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Original article

Early development of acute kidney injury is an independent predictor of in-hospital mortality in patients with acute myocardial infarction

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ABSTRACT

Background: Acute kidney injury (AKI) often occurs in patients with acute myocardial infarction (AMI), and is associated with adverse outcomes. However, it remains unclear how timing of AKI affects it. This study assessed impact of timing of AKI on prognosis after AMI.
Methods: This study consisted of 760 patients with AMI who were admitted within 48 h after symptom onset. AKI was diagnosed as increase in creatinine ≥0.3 mg/dl or ≥50% within any 48 h after admission. Patients were classified into 3 groups according to the occurrence and timing of AKI: no-AKI, early-AKI (within 48 h after admission) and late-AKI (>48 h). Early-AKI was classified into transient early-AKI, defined as creatinine returning to the level below the criteria of AKI, and persistent early-AKI.
Results: Early-AKI occurred in 64 patients (9%) and late-AKI in 32 patients (4%). Patients with early-AKI had significantly higher mortality (35%) than those with late-AKI (7%, $p < 0.001$) and no-AKI (3%, $p < 0.001$). Multivariate analysis showed early-AKI was an independent predictor of in-hospital mortality (OR: 3.38, 95% CI: 1.30–8.76, $p = 0.013$), but late-AKI was not. Among patients with early-AKI, mortality was significantly higher even if AKI was transient (23%, $p < 0.001$). Patients with persistent early-AKI had the highest mortality (66%, $p < 0.001$).
Conclusions: Early-AKI was associated with worse outcome. Even if renal function once returned to baseline level, patients with early-AKI tended to be at high risk of mortality.

Introduction

Acute kidney injury (AKI) is a severe state that occurs in various situations and is associated with poor prognosis in serious diseases [1–4]. Acute myocardial infarction (AMI) is one of the critical conditions where AKI is likely to occur. Although several studies have demonstrated that AKI is associated with worse outcomes after AMI, it is often under-recognized in the clinical setting [5]. Importantly, severity and timing of AKI differ from patient to patient. It has been reported that the severity of AKI correlates with mortality and morbidity [6–8]. However, it remains unclear how the timing and course of AKI affect prognosis of patients with AMI. This study aimed to assess the timing of AKI, its course, and its impact on in-hospital mortality in patients with AMI.

Methods

From January 2007 to June 2012, 798 consecutive patients who were admitted to the National Cerebral and Cardiovascular Center in Japan within 48 h after the onset of symptoms were

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prospectively enrolled to the observational single-center registry and were retrospectively analyzed. In this registry, AMI was defined by a combination of 2 of the 3 following: chest pain longer than 30 min, electrocardiographic signs, and elevation of serum creatinine kinase more than twice the upper normal limit. For the present analysis, we excluded patients on dialysis (n = 12) or those with missing initial creatinine and admission data (n = 26). Finally, this study consisted of the remaining 760 patients who constituted the study population.

Emergency coronary angiography was performed in most of the cases, if indicated. Selective coronary angiography was performed in multiple projections before the initiation of reperfusion therapy. Immediately after diagnostic angiography, reperfusion therapy was performed mostly with primary percutaneous coronary intervention (PCI) with stent. The allocation of angiography or PCI was not randomized and was based on the physician's decision.

The study protocol was approved by the institutional review board of National Cerebral and Cardiovascular Center, and was conducted in accordance with regulations governing epidemiological studies issued by the Ministry of Health, Labor, and Welfare of Japan.

Blood samples, including creatinine and other baseline laboratory parameters had to be obtained on admission. Creatinine was measured every day for the first three days, and then at least every two days during the first week after hospital admission. Creatine kinase (CK) was measured every 3 h until it reached its peak value.

According to criteria proposed by AKI network, AKI was defined as increase in serum creatinine of more than or equal to 0.3 mg/dl or increase to more than or equal to 150% from baseline within any 48 h during hospital days [9]. Patients were divided into 3 groups according to the occurrence and timing of AKI development: no-AKI, early-AKI (AKI occurring within 48 h after admission), and late-AKI (>48 h). Early-AKI was further divided into transient early-AKI and persistent early-AKI. AKI was thought to be transient if serum creatinine decreased to the level less than that of AKI network criteria.

Patient baseline characteristics, treatment, and interventions were summarized by AKI category. Categorical data were reported as proportions and continuous data as mean values with standard deviations. Statistical analysis was performed with the Chi-square test or Fisher exact for categorical variables. The t test was used for continuous variables. To evaluate the difference of three groups, we used Kruskal–Wallis test. Logistic regression analysis was used to obtain odds ratio (OR) and 95% confidence interval (CI) for the development of AKI. In multivariate analysis, the association between early-AKI and in-hospital mortality was adjusted for variables (age, Killip class, systolic blood pressure, heart rate, peak CK, eGFR (estimated glomerular filtration rate (ml/min/1.73 m^2)), creatinine, emergency PCI, diabetes mellitus, and late-AKI) that were predictors of in-hospital mortality. Because peak CK was not obtained in 9 patients (1.2%), 2 models of multivariate analysis were used. Chronic kidney disease (CKD) was defined as eGFR < 60. We used the JMP statistical package (version 10.0, SAS institute, Cary, NC, USA). A significance level of 0.05 was used and two-tailed tests were applied.

Results

AKI developed in 96 patients (13%). Baseline characteristics of patients with AKI and no-AKI are shown in Table 1. AKI was associated with older age, lower blood pressure, faster heart rate, more diabetes, lower eGFR, higher creatinine, more Killip class ≥2, and higher peak CK. Most patients underwent emergency coronary angiography (93%) and primary PCI (86%), with no significant difference between patients with AKI and no-AKI.

Table 1
Baseline characteristics of AMI patients with and without AKI.

	AKI (+) n = 96 (13%)	AKI (−) n = 664 (87%)	p-Value
Age	72.8 ± 11.8	67.3 ± 12.9	<0.001
Male	70 (73%)	472 (71%)	0.71
BMI	23.6 ± 4.6	23.5 ± 3.6	0.83
Systric blood pressure (mm Hg)	121.7 ± 36.3	132.2 ± 27.3	0.0012
Heart rate (bpm)	82.7 ± 27.6	74.8 ± 20.4	0.001
Hypertension	72 (75%)	440 (66%)	0.082
Dyslipidemia	40 (42%)	375 (56%)	0.006
Diabetes mellitus	51 (53%)	204 (31%)	<0.001
Current smoking	33 (34%)	223 (34%)	0.88
eGFR (ml/min/1.73 m^2)	46 ± 27	70 ± 24	<0.001
Creatinine (mg/dl)	1.78 ± 1.79	1.01 ± 1.23	<0.001
STEMI	81 (84%)	544 (82%)	0.55
Killip ≥ 2	52 (54%)	110 (16%)	<0.001
Onset to admission (h)	6.6 ± 8.4	7.6 ± 10.1	0.37
Emergency Angiography	86 (90%)	622 (94%)	0.14
Primary PCI	77 (80%)	577 (87%)	0.091
Peak creatine kinase (IU/l) (n = 751)[a]	4948 ± 5034	2665 ± 2621	<0.001

Categorical variables are expressed as n (%) and continuous variables as mean ± SD.
STEMI = ST elevation myocardial infarction; PCI = paracutaneous coronary intervention; eGFR = estimated glomerular filtration rate.
[a] Peak creatine kinase was not obtained in 9 patients.

In-hospital mortality of the entire study patient population was 5.7%. Mortality was significantly higher in patients with AKI than in those with no-AKI (25% versus 3%, $p < 0.001$).

Median duration from the onset of AMI to the development of AKI was 2 days (Fig. 1). Early-AKI developed in 64 patients (9%) and late-AKI in 32 patients (4%). There was no significant difference in baseline variables between patient with early-AKI, late-AKI, and no-AKI, except for higher age, lower blood pressure, faster heart rate, less dyslipidemia, more diabetes mellitus, higher peak CK, lower eGFR, and more Killip class ≥2 in patients with AKI (Table 2). In-hospital mortality of patients with early-AKI and late-AKI was 35% and 7%, respectively. Mortality of patients with early-AKI was significantly higher not only than no-AKI ($p < 0.001$) but also than late-AKI ($p = 0.002$). The difference in mortality was not statistically significant between late-AKI and no-AKI (Fig. 2). This trend was consistently observed when patients were divided according to the presence or absence of shock (Killip class 4 or not), chronic kidney disease, diabetes mellitus, or peak CK above its median value (2002 IU/l) (Fig. 3).

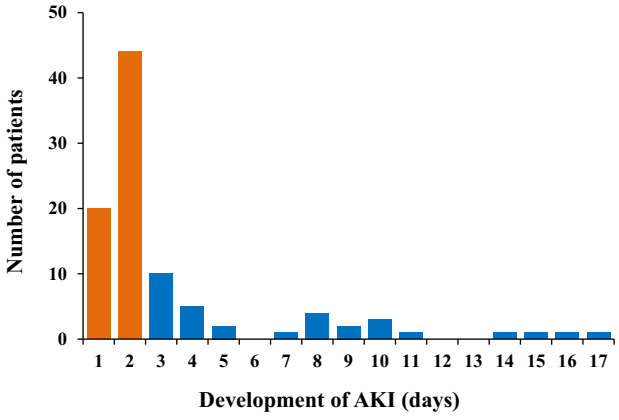

Fig. 1. The relation between number of patients and date of acute kidney injury (AKI) occurrence. Median duration from the onset of acute myocardial infarction to the development of AKI was 2 days. Orange bar revealed number of patients with early-AKI, and blue bar those with late-AKI.

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