Acute Kidney Injury and Acute Myocardial Infarction – Importance of Admission Hyperglycemia –

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In this issue of the Journal, Moriyama et al report that acute kidney injury (AKI) developed in 13% of patients after acute myocardial infarction (AMI) and that AKI was associated with higher in-hospital mortality after AMI.¹ This report is important because they show that admission hyperglycemia was an independent risk factor for AKI in patients with AMI. And patients with admission hyperglycemia were at higher risk of death during hospitalization for AMI, regardless of the use of coronary angiography (CAG) or primary percutaneous coronary intervention (PCI).

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Admission hyperglycemia in patients with AMI is common and strongly associated with increased mortality in both the short- and long-term period (Figure).^{2,3} Deckers et al³ investigated 11,324 consecutive patients admitted for AMI from 1985 to 2008 and reported that the prevalence of hyperglycemia increased from 26% in the 1980s to 49% in the 2000s. The prevalence of hyperglycemia primarily increased in patients without diabetes mellitus. Acute hyperglycemia causes several unfavorable effects that contribute to the poor prognosis through oxidative stress, inflammation, apoptosis, endothelial dysfunction,

hypercoagulability, platelet hyperactivity, impaired ischemic preconditioning, impaired microcirculation, and so on.² However, there are several issues to be clarified regarding the effect of hyperglycemia in AMI. The significant association between admission hyperglycemia and AKI in patients with AMI suggests a new insight into one of the mechanisms of the poor prognosis of AMI patients with admission hyperglycemia. The limitations of this study are as follows: a single-center and retrospective study, and only the short-term prognosis (in-hospital mortality) was investigated. Further investigations into the long-term prognosis after AKI, the changes in renal function in patients with AKI, and the relationship between the volume of contrast media used during emergency CAG or primary PCI and AKI should be addressed.

There are many definitions of AKI. In 2004, the Acute Dialysis Quality Initiative group developed a new definition known as RIFLE (acronym indicating Risk of renal dysfunction, Injury to the kidney, Failure of kidney function, Loss of kidney function and End-stage kidney disease).⁴ The definition of AKI was increased serum creatinine (SCr) ≥ 1.5 -fold, glomerular filtration rate (GFR) decrease $>25\%$, or urine output $<5 \text{ ml} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$ for 6 h. In 2005, the Acute Kidney Injury Network (AKIN) was established, and modified definition and diagnostic criteria

Figure. In-hospital mortality rate in relation to admission blood glucose level in patients with acute myocardial infarction: 2% in patients with glucose $\leq 5 \text{ mmol/L}$, 3% in patients with glucose 5–7 mmol/L, 5% in patients with glucose 7–9 mmol/L, 10% in patients with glucose 9–11 mmol/L, 12% in patients with glucose 11–13 mmol/L and 18% in patients with glucose $>13 \text{ mmol/L}$; all $P < 0.001$. (Reproduced with permission from Ishihara M.²)

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Table. Acute Kidney Injury Definition and Staging in the KDIGO Guideline

Definition	<ul style="list-style-type: none"> • Increase in SCr by ≥ 0.3 mg/dl within 48 h or • Increase in SCr to ≥ 1.5-fold baseline, which is known or presumed to have occurred within the prior 7 days or • Urine volume <0.5 ml $\cdot$ kg⁻¹ $\cdot$ h⁻¹ for 6 h. 	
Staging	SCr	Urine output
Stage 1	1.5–1.9-fold baseline or ≥ 0.3 mg/dl increase	<0.5 ml $\cdot$ kg ⁻¹ $\cdot$ h ⁻¹ for 6–12 h
Stage 2	2.0–2.9-fold baseline	<0.5 ml $\cdot$ kg ⁻¹ $\cdot$ h ⁻¹ for ≥ 12 h
Stage 3	3.0-fold baseline or Increase in SCr to ≥ 4.0 mg/dl or Initiation of renal replacement therapy or In patients <18 years, decrease in eGFR to <35 ml $\cdot$ min ⁻¹ per 1.73 m ²	<0.3 ml $\cdot$ kg ⁻¹ $\cdot$ h ⁻¹ for ≥ 24 h or Anuria for ≥ 12 h

eGFR, estimated glomerular filtration rate; KDIGO, Kidney Disease: Improving Global Outcomes; SCr, serum creatinine. (Reproduced with permission from KDIGO Acute Kidney Injury Work Group.⁶)

(AKIN criteria) were proposed in 2007.⁵ An abrupt (within 48 h) reduction in kidney function currently defined as an absolute increase in SCr ≥ 0.3 mg/dl, a percentage increase in SCr ≥ 1.5 -fold, or a reduction in urine output (documented oliguria <0.5 ml $\cdot$ kg⁻¹ $\cdot$ h⁻¹ for more than 6 h). And Kidney Disease: Improving Global Outcomes (KDIGO) made a clinical practice guideline for AKI in 2012 (Table).⁶ On the other hand, AKI caused by iodinated contrast media is called contrast-induced AKI (CI-AKI) and is a common and potentially serious complication after the administration of contrast media. Risk markers of CI-AKI are chronic kidney disease, diabetes mellitus, volume depletion, nephrotoxic drugs, hemodynamic instability, and other comorbidities.⁷ Several definitions for CI-AKI have been used, and the definition influences the incidence and prognosis of CI-AKI.^{8,9} Recently, the Japan Radiological Society, Japanese Circulation Society, and Japanese Society of Nephrology established a guideline on the use of iodinated contrast media in patients with kidney disease.¹⁰ In this guideline, contrast-induced nephropathy is defined as an increase in SCr levels by ≥ 0.5 mg/dl or $\geq 25\%$ from baseline within 72 h of contrast radiography using iodinated contrast media.

Patients with AMI have many comorbidities for developing AKI such as hemodynamic instability, cardiogenic shock, renal hypotension, or large volume of contrast media and lack of sufficient hydration at primary PCI.^{11,12} Especially, contrast media used in emergency CAG or primary PCI are an important risk factor of AKI. The pathogenesis of CI-AKI is complex and not fully understood. Contrast media induce intense and prolonged vasoconstriction at the corticomedullary junction of the kidney, as well as the impaired autoregulatory capacity of the kidney through a loss of nitric oxide production.^{13,14} In the setting of primary PCI, sufficient hydration to prevent CI-AKI is not necessarily easy. Morikawa et al reported the effectiveness of atrial natriuretic peptide for the prevention of CI-AKI in patients with chronic kidney disease.¹⁵ However, atrial natriuretic peptide was initiated 4–6 h before angiography and continued for 48 h in that study. Therefore, whether atrial natriuretic peptide treatment is effective or not in the acute setting remains to be clarified. In patients with AMI and admission hyperglycemia, careful monitoring of renal function is required because admission hyperglycemia could be an independent predictor for AKI in AMI patients. New ways of management, including more strict glycemic control, to prevent AKI in patients with AMI should be explored in the future.

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