Abnormal glucose metabolism is an important prognostic factor in patients with acute myocardial infarction (AMI). Blood glucose levels are commonly elevated, and raised blood glucose concentrations on admission are reported to be associated with increased mortality in patients with AMI. Elevated fasting glucose is also reported to be associated with 30-day mortality in AMI patients. Furthermore, hypoglycemia on admission is associated with higher in-hospital and long term mortality compared with euglycemia. Acute glycemic fluctuations from peaks to nadirs, so-called glycemic variability (GV), has been also reported as associated with higher risk for mortality in patients with diabetes mellitus (DM). However, there are insufficient data regarding the association of GV and clinical outcomes in AMI patients.

In this issue of the Journal, Gohbara et al prospectively evaluate the clinical effect of GV as determined by a continuous glucose monitoring system (CGMS) on left ventricular (LV) remodeling in 69 patients with a first reperfused ST-segment elevation MI within 12h of onset. LV remodeling was assessed by cardiac magnetic resonance imaging (CMR). Patients were equipped with a CGMS when in a stable phase after admission and underwent repeat CMR at baseline and 7 months follow-up. One of the important points in this study is that the authors excluded those with medications for DM to eliminate the effect of such medications on GV. The baseline HbA1c level was not so high and was equivalent between the high mean amplitude of glycemic excursion (MAGE) group (Group H) and low MAGE group (Group L) (5.9±0.6 vs. 5.8±0.4, P=0.3). Glucose level on admission was also not significantly different between the 2 groups. Regarding the myocardial damage in the acute phase, there was no significant difference between groups H and L with regard to the mean extent of core (19±9% LV mass vs. 20±1% LV mass, P=0.518) and peak creatine phosphokinase levels.

At 7-month follow-up, the HbA1c levels were also not significantly different between the 2 groups (6.0±0.5 vs.
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5.9±0.5, P=0.42). However, LV remodeling had more frequently occurred in group H than in group L (56% vs. 11%, P<0.001). Multivariate analysis showed that higher MAGE was an independent predictor of LV remodeling in the chronic phase (odds ratio, 13.999; 95% CI, 3.059 to 64.056; P=0.001). B-type natriuretic peptide (BNP) levels at 7-month follow-up were also significantly higher in group H than in group L (74±55 vs. 44±34, P=0.02), although the baseline BNP levels were not significantly different. These results suggest that GV could have influenced LV remodeling in the chronic phase in patients with AMI regardless of the level of HbA1c or glucose on admission.

The risk for complications in patients with glycemic dysfunction could be determined by the excessive glycation and generation of oxidative stress that are activated by 3 main glycemic disorders: hyperglycemia both at fasting and during the postprandial period and acute glucose fluctuations (Figure 1).7 Glucose fluctuations are reported to be a more specific triggering effect on oxidative stress than chronic sustained hyperglycemia.8 Therefore, activation of oxidative stress by acute glucose fluctuations is considered to be the underlying mechanism of LV remodeling in patients with higher MAGE in the current study.

LV remodeling after AMI is an important prognostic factor because remodeling leads to progressive LV dilatation and impaired cardiac function, resulting in chronic heart failure. Infarct size and persistent occlusion of the coronary artery have been reported as the 2 main factors promoting LV remodeling.5,10 Oxidative stress is also reported as a cause of LV remodeling after AMI. Fuji et al reported that oxidative stress could play an important role in the development and progression of LV remodeling after AMI.11 Plasma oxidized low-density lipoprotein levels 7 days after AMI significantly correlated with LV end-diastolic volume (115±7 mL; r=0.54, P=0.0025) and end-systolic volume (58±5 mL; r=0.49, P=0.008) 3 months after the AMI. Teraguchi et al investigated the effect of glucose fluctuation on myocardial salvage following successful recanalization of primary AMI.12 Acute-phase GV monitored approximately 24h after the onset of AMI negatively correlated with the myocardial salvage index (MSI; r=-0.49, P=0.01) in both the DM and non-DM group (Figure 2). Glucose fluctuations during the acute phase of AMI affected the MSI, indicating that manipulation of GV could be a potential therapy for salvaging ischemic damage.

In recent clinical trials aiming to reduce the HbA1c levels in patients with DM, there was failure to improve cardiovascular outcomes.13,14 As the HbA1c level reflects the average glucose level rather than GV, GV would be a more important and appropriate therapeutic target than the HbA1c level for reducing cardiovascular events in patients with glycemic dysfunction.

In conclusion, higher level of MAGE could be the cause of LV remodeling in the chronic phase in patients with AMI regardless of the level of HbA1c. GV could be the target for treatment in AMI patients to salvage the myocardial damage and improve clinical outcomes.

Disclosures
None.

References