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Original article

Clinical impact of acute hyperglycemia on development of diabetes mellitus in non-diabetic patients with acute myocardial infarction

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ABSTRACT

Background: Acute hyperglycemia (AH) after the onset of acute myocardial infarction (AMI) is a manifestation of transient abnormal glucose metabolism that may reflect AMI severity, and thus be a predictor of poor prognosis. However, it remains unknown whether AH may predict development of *de novo* diabetes mellitus (dn-DM) in non-diabetic AMI patients.

Methods and results: Among AMI patients registered in the Osaka Acute Coronary Insufficiency Study between 1998 and 2007, we investigated hospital records of 1493 patients who had an admission glycated hemoglobin A1c (HbA1c) level of ≤6.0% and were subjected to glycometabolic profiling after survival discharge. dn-DM was defined as initiation of diabetic medication or documentation of an HbA1c level of ≥6.5% during the 5-year follow-up period. AH, defined as an admission serum glucose level of ≥200 mg/dl, was observed in 133 (8.9%) patients. dn-DM development was more frequent in post-AMI patients with AH than those without [24.8% vs 12.0%, adjusted hazard ratio (HR) 1.776, $p = 0.021$], particularly among patients with an HbA1c of <5.6% on admission. Treatment with angiotensin-converting enzyme inhibitors or angiotensin receptor blockers was associated with a reduced incidence of dn-DM in patients with AH (adjusted HR 0.397, $p = 0.031$).

Conclusion: Admission AH was a predictor of dn-DM in non-diabetic post-AMI patients. Renin–angiotensin system inhibitors were associated with reduced incidence of dn-DM in post-AMI patients with AH.

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Introduction

Numerous studies have identified an association between diabetes mellitus (DM) and the incidence or development of coronary heart disease (CHD), including acute myocardial infarction (AMI) [1–8]. It has been reported that patients with a recent myocardial infarction have a higher annual incidence rate of impaired fasting glucose and DM than the general population [9], suggesting that AMI may be a DM risk equivalent [10]. In addition, evidence suggests that post-AMI patients who develop DM are at high risk of adverse events [10]. As these findings indicate that diabetic individuals with CHD have worse morbidity and mortality than non-diabetic CHD patients [11,12], risk stratification in the clinical setting for the development of *de novo* DM (dn-DM) is expected to improve mortality in post-AMI patients. To date, however, few predictive markers for the development of dn-DM after AMI have been identified.

In the present study, we investigated the clinical impact of acute hyperglycemia (AH) on the development of dn-DM and pharmacological modification in post-AMI patients. AH, which is often observed in both non-diabetic and diabetic AMI patients [13,14], is considered to be a manifestation of transient abnormal glucose metabolism that is induced during the acute phase of myocardial infarction (MI) [13–18]. Although a few studies have reported a relationship between AH and adverse clinical outcomes after AMI, the association between AH and development of dn-DM after survival discharge for AMI was unclear. Thus, in the present study, we examined a hypothesis that AH is a predictor for the development of dn-DM in post-AMI patients by reviewing the database of the Osaka Acute Coronary Insufficiency Study (OACIS) registry.

Methods

The OACIS registry

The OACIS is a prospective multicenter observational study involving 25 hospitals from the Osaka region of Japan that record demographic, procedural, and outcome data, and collect blood samples from AMI patients. The OACIS is registered with the University Hospital Medical Information Network Clinical Trials Registry, Japan (ID: UMIN000004575). A detailed description of the OACIS has been published elsewhere [19–22]. The OACIS study protocol was approved by the ethical committee of each participating hospital and written informed consent was provided by all patients at the time of registration. The OACIS registry is designed to collect uniform prospective data that can be used to assess clinical variables, therapeutic procedures, and clinical events in AMI patients. The diagnosis of AMI required 2 of the following 3 criteria to be met: (1) a history of central chest pressure, pain, or tightness lasting for 30 min or more, (2) ST-segment elevation greater than 0.1 mV in at least 1 limb lead or 2 precordial leads, and (3) an increase of serum creatine kinase (CK) concentration to more than twice the upper limit of normal. All patients presenting within one week after the onset of AMI were registered prospectively after the diagnosis of AMI was made.

Study population

Of 8025 consecutive AMI patients registered in the OACIS between April 1998 and December 2007, patients who fulfilled the following criteria were enrolled in the present study: (1) non-diabetic patients discharged alive; (2) assessment of development of dn-DM during a five-year follow-up period; and (3) plasma glucose and glycated hemoglobin A1c (HbA1c) levels were measured on admission. To minimize the influence of pre-existing DM on hyperglycemia, we excluded patients with an HbA1c > 6.0% on admission. A total of 1493 patients fulfilled the inclusion criteria. These patients were divided into 2 groups according to whether they had a plasma glucose concentration of ≥200 mg/dl (AH group; $n = 133$) or <200 mg/dl (non-AH group; $n = 1360$) on admission. The AH and non-AH groups were further divided into subgroups based on treatment with angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs) at the time of discharge.

Data collection

Investigative cardiologists and trained research nurses recorded data on the demographic variables, medical history, therapeutic procedures, and clinical events of each patient during hospitalization. Information was obtained from the medical records and by direct interview of the patients, family members, and treating physicians.

Primary endpoints and definitions

The primary end-point for this study was the development of dn-DM after survival discharge for AMI. Patients were considered to have developed dn-DM if any of the following occurred during the 5-year follow-up period: (1) a clinical diagnosis of DM was reported. If the investigator or the treating physician reported a clinical diagnosis of DM, or if the patients had started chronic medical treatment with insulin or an oral anti-diabetic agent; or (2) if the patient had an HbA1c level of ≥6.5% during the 5-year follow-up period.

Hypertension was defined as a history of systolic blood pressure ≥ 140 mmHg, diastolic blood pressure ≥ 90 mmHg, or antihypertensive therapy. Hyperlipidemia was defined as fasting total cholesterol ≥ 220 mg/dl, fasting triglycerides ≥ 150 mg/dl, or antilipidemial therapy. Smoking was defined as currently smoking or a history of smoking. A history of DM was defined as patients who had been diagnosed or were being treated for DM (diet, tablets, or insulin) before admission, during hospitalization, or at the time of discharge, and as those patients with an admission HbA1c of >6.0%. In this study, the HbA1c values of patients were converted by calculating formula of the National Glycohemoglobin Standardization Program (NGSP) from Japanese conventional HbA1c value (JDS value).

Statistical analysis

Data are expressed as the mean ± standard deviation (SD) or median with 25th and 75th percentiles for continuous variables, while qualitative data are presented as numbers or percentages. Differences in continuous variables between groups were compared by the Student's *t*-test or the Mann–Whitney *U*-test, while categorical variables were compared by the chi-square test. To assess the association between patient characteristics and AH, we used an adjusted logistic regression model. Survival curves were constructed by the Kaplan–Meier method and the significance of differences in survival was assessed by the log-rank test. To reduce the impact of treatment selection bias and potential confounding, a Cox proportional-hazards regression model was used during the assessment of predictors for the development of dn-DM and for the association between the reduced incidence of development of dn-DM and treatment with ACE inhibitors or ARBs. The variables included in the regression model were age, male gender, body mass index (BMI), history of hypertension, history of hyperlipidemia, smoking, Killip classification on hospital admission, HbA1c on admission, peak CK of >3000 IU/L, ST-elevation MI, and major medication at hospital discharge. Data analysis was performed using SPSS statistical software (version 19.0; SPSS Japan

Table 1
Clinical baseline characteristics of study patients with and without acute hyperglycemia.

Variable	Acute hyperglycemia (−) Plasma glucose < 200 mg/dl (*N* = 1360)	Acute hyperglycemia (+) Plasma glucose ≥ 200 mg/dl (*N* = 133)	*p*-Value
Clinical characteristic			
Men (%)	76.2	68.4	0.057
Age (years)	65.3 ± 12.0	68.1 ± 11.3	0.008
Body mass index (kg/m^2)	23.4 ± 3.5	22.6 ± 3.2	0.016
Hypertension (%)	54.6	57.3	0.582
Hyperlipidemia (%)	41.8	34.6	0.135
Smoking (%)	64.7	57.3	0.105
Familial history of diabetes (%)	16.8	17.5	0.876
ST elevation myocardial infarction (%)	83.8	87.1	0.383
Killip classification ≥ II (%)	10.2	36.0	<0.001
Peak CK > 3000 IU/L (%)	35.6	56.3	<0.001
Onset to admission (h)	3.5 (1.5–13.5)	2.0 (1.0–7.4)	0.393
HbA1c at admission (%)	5.54 ± 0.3	5.51 ± 0.3	0.387
Glucose levels at admission (mg/dl)	129.9 ± 27.7	258.5 ± 62.0	<0.001
Fasting glucose levels at discharge (mg/dl)	92.8 ± 14.3	96.8 ± 30.0	0.124
Re-perfusion therapy (%)	89.9	93.2	0.283
PCI (%)	86.9	91.7	0.132
Medications at hospital discharge			
Antiplatelets (%)	98.0	99.2	0.506
ACE inhibitors or ARBs (%)	75.6	72.9	0.527
Beta-blockers (%)	48.0	51.9	0.414
Ca-antagonists (%)	18.7	10.5	0.018
Statins (%)	36.9	30.1	0.131
Diuretics (%)	24.4	42.9	<0.001
Nitrates (%)	36.9	51.1	0.002

Data are shown as median or mean ± SD for continuous variables and percentages for dichotomous variables.
CK, creatine kinase; HbA1c, glycated hemoglobin A1c; PCI, percutaneous coronary intervention; ACE, angiotensin-converting enzyme; ARB, angiotensin receptor, blocker.

Inc., Tokyo, Japan). For all analyses, statistical significance was defined as $p < 0.05$ and p for interaction < 0.1.

Results

Of the total 1493 AMI patients included in the study, 196 (13.1%) were newly diagnosed with DM during the mean follow-up period of 924 days. The clinical characteristics and major medications at hospital discharge for the study patients based on the occurrence of AH are listed in Table 1. Patients with AH were older, had a lower BMI, a higher prevalence of Killip classification on admission ≥II, and larger MI, as determined by peak CK, than those without AH. Furthermore, patients with AH were more often treated with diuretics and nitrates at discharge, but were prescribed Ca-antagonists significantly less often. No differences between the two AMI patient groups were seen in HbA1c on admission, or fasting glucose levels and other medications at discharge. In adjusted logistic regression analysis, AH was associated with higher Killip classification and larger MI, but was not associated with HbA1c on admission (Table 2).

Fig. 1 presents Kaplan–Meier curves for the development of dn-DM in patients with and without AH. Patients with AH had a higher incidence of dn-DM than those in the non-AH group (24.8% vs 12.0%, respectively; log-rank test $p < 0.001$).

In the multivariate analysis, AH was found to be an independent predictor for the development of dn-DM in post-AMI patients (Table 3). After adjustment for age and male gender (Model 1), the hazard ratio (HR) was 2.210 (95% CI 1.518–3.219). With further adjustment for age, male gender, history of hypertension, hyperlipidemia, smoking, HbA1c on admission, BMI, Killip classification on hospital admission, peak CK > 3000 IU/L, ST-elevation MI, and medication at hospital discharge (Model 4), AH remained as an independent predictor for the development of dn-DM in post-AMI patients (HR 1.776, 95% CI 1.092–2.890, $p = 0.021$).

To minimize the influence of pre-existing DM on the apparent predictive value of hyperglycemia, we also analyzed the association between AH and dn-DM according to HbA1c levels on admission,

Table 2
Patient characteristics associated with acute hyperglycemia on admission after acute myocardial infarction.

Characteristic	Association with acute hyperglycemia		
	Odds ratio	95% CI	*p*-Value
Men	0.843	0.489–1.451	0.537
Age (per 1 year of age)	1.011	0.989–1.034	0.345
Body mass index (per 1 kg/m^2)	0.950	0.887–1.019	0.151
Hypertension	1.173	0.747–1.841	0.489
Hyperlipidemia	0.903	0.572–1.424	0.660
Smoking	1.071	0.643–1.783	0.793
ST elevation myocardial infarction	1.067	0.560–2.032	0.844
Killip classification	1.909	1.502–2.425	<0.001
Peak CK > 3000 IU/L	1.831	1.164–2.879	0.009
Onset to admission time (per 1 h)	0.989	0.974–1.005	0.186
HbA1c at admission (per 0.1%)	0.967	0.905–1.035	0.334

CK, creatine kinase; HbA1c, glycated hemoglobin A1c.

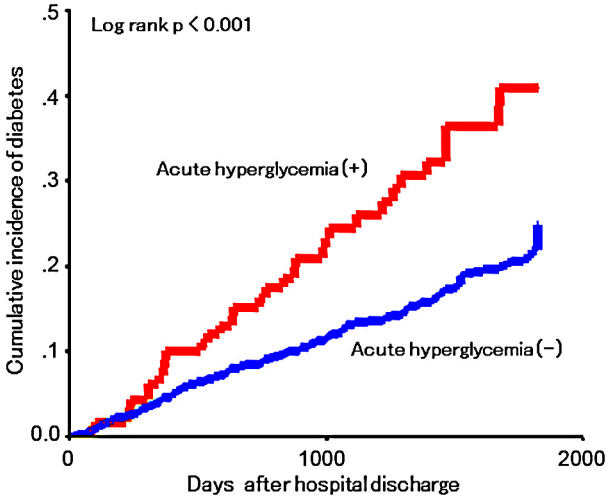

Fig. 1. Kaplan–Meier estimates for the development of *de novo* diabetes mellitus in acute myocardial infarction patients with and without acute hyperglycemia.

Table 3
Association between acute hyperglycemia and development of *de novo* diabetes mellitus.

	Development of *de novo* diabetes mellitus		
	Hazard ratio	95% CI	*p*-Value
Univariate	2.069	1.423–3.008	<0.001
Multivariate			
Model 1	2.210	1.518–3.219	<0.001
Model 2	2.148	1.423–3.240	<0.001
Model 3	1.665	1.032–2.686	0.037
Model 4	1.776	1.092–2.890	0.021

Model 1: adjusted for age and male gender; Model 2: adjusted for age, male gender, history of hypertension, hyperlipidemia, smoking, HbA1c on admission, and body mass index; Model 3, adjusted for age, male gender, history of hypertension, hyperlipidemia, smoking, HbA1c on admission, body mass index, Killip classification on hospital admission, peak CK > 3000 IU/L, and ST-elevation myocardial infarction; Model 4, adjusted for age, male gender, history of hypertension, hyperlipidemia, smoking, HbA1c on admission, body mass index, Killip classification on hospital admission, peak CK > 3000 IU/L, ST-elevation myocardial infarction, and medication at hospital discharge.
CI, confidence interval; CK, creatine kinase; HbA1c, glycated hemoglobin A1c.

using a value of 5.6% (Fig. 2). In post-AMI patients with lower HbA1c levels (<5.6%), a stronger association was detected between AH and the development of dn-DM than in those patients with higher HbA1c levels (≥5.6%) (adjusted *p* for interaction = 0.062).

We next evaluated the pharmacological modification of this impact in post-AMI patients and found that inhibition of the renin–angiotensin system (RAS) might have attenuated the risk of AH on the development of dn-DM after AMI. Table 4 shows the clinical characteristics, as well as the treatments and major medications at hospital discharge, of AH group patients treated with and without RAS inhibitors, such as ACE inhibitors and ARBs, at hospital discharge. Patients treated with RAS inhibitors at discharge had slightly lower HbA1c levels on admission than AH group patients not receiving RAS inhibitors. However, no differences between the two groups were detected in the other examined parameters.

Fig. 3 presents Kaplan–Meier curves for the development of dn-DM among post-AMI patients treated with and without RAS inhibitors according to the prevalence of AH. In patients without AH, no differences in the development of dn-DM were found based on treatment with RAS inhibitors. In contrast, in patients with AH, a lower incidence of dn-DM was detected in those treated with RAS inhibitors at discharge than those without (20.6% vs 36.1%, respectively; log-rank test $p = 0.010$). The multivariate analysis revealed that treatment with RAS inhibitors was associated with a reduced incidence of development of dn-DM (HR 0.397, 95% CI 0.171–0.921, $p = 0.031$) in AH group patients, whereas no association was found in non-AH group patients (adjusted *p* for interaction = 0.055; Table 5).

Discussion

The present study revealed that AH after the onset of AMI may be an independent predictor of dn-DM development in non-diabetic AMI patients. Our findings also suggest that inhibition of the RAS may attenuate the risk of dn-DM in the secondary prevention setting after AMI with AH.

AH is a common feature during the early phase after AMI, even in non-diabetic patients [13,14,18]. A number of studies have identified an association between AH and poor prognosis following AMI, particularly in non-diabetic patients [13–15,17,23,24]. AH is reported to be a manifestation of transient abnormal glucose metabolism that is possibly induced by the acute release of catecholamine, cortisol, and cytokines in the acute stage of MI [25–33]. Although several studies have reported a relationship between AH and adverse clinical outcomes after AMI, the association between AH and development of dn-DM after survival discharge for AMI was unclear prior to the present study. In the present study, the univariate analysis revealed that patients with AH had a 2.1-fold higher risk for the development of dn-DM. Furthermore, multivariate analysis demonstrated that this association remained unchanged in four different statistical models, even after adjustment for age, male gender, history of hypertension, hyperlipidemia, smoking, HbA1c and Killip classification on admission, BMI, peak CK > 3000 IU/L, ST-elevation MI, and medication at hospital discharge, which included statins, ACE inhibitors, ARBs, beta-blockers, nitrates, and diuretics. Based on these analyses, we may conclude that AH during the acute stage of AMI is a useful predictor for the development of dn-DM in patients without a previous diagnosis of DM.

Although the mechanisms underlying the relationship between AH and dn-DM in post-AMI patients remain unclear, there are

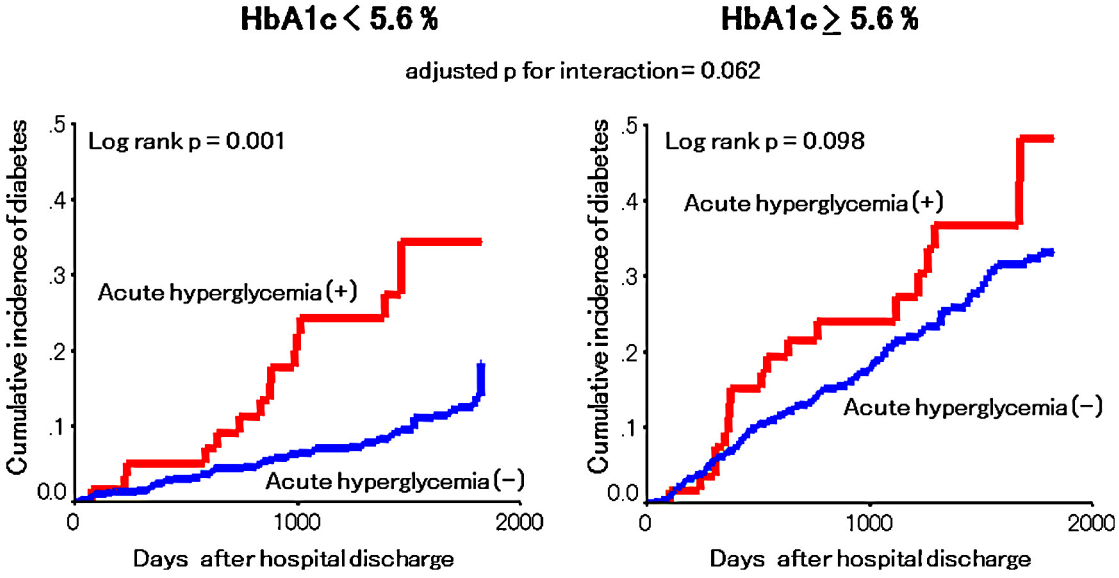

Fig. 2. Kaplan–Meier estimates for the development of *de novo* diabetes mellitus in acute myocardial infarction patients with and without acute hyperglycemia, as determined by glycated hemoglobin (HbA1c) values on admission of 5.6%.

Table 4
Clinical baseline characteristics of acute myocardial infarction patients with acute hyperglycemia based on ACE inhibitors or ARBs at discharge.

Variable	Acute hyperglycemia (+) ACE inhibitors or ARBs (−) (*N* = 36)	Acute hyperglycemia (+) ACE inhibitors or ARBs (+) (*N* = 97)	*p*-Value
Clinical characteristic			
Men (%)	69.4	68.0	1.000
Age (years)	69.1 ± 13.4	67.7 ± 10.5	0.519
Body mass index (kg/m^2)	22.6 ± 4.0	22.7 ± 2.9	0.934
Hypertension (%)	47.2	61.1	0.170
Hyperlipidemia (%)	25.0	38.3	0.216
Smoking (%)	61.8	55.7	0.554
Familial history of diabetes (%)	5.6	21.0	0.172
ST elevation myocardial infarction (%)	91.4	85.6	0.558
Killip classification ≥ II (%)	41.2	34.1	0.905
Peak CK > 3000 IU/L (%)	62.5	54.0	0.532
Onset to admission (h)	1.8 (1.0–8.5)	2.0 (1.0–5.7)	0.987
HbA1c at admission (%)	5.6 ± 0.3	5.5 ± 0.3	0.039
Glucose levels at admission (mg/dl)	257.9 ± 65.7	258.7 ± 60.9	0.949
Fasting glucose levels at discharge (mg/dl)	102.4 ± 33.3	94.2 ± 15.8	0.132
Re-perfusion therapy (%)	94.4	92.8	1.000
PCI (%)	91.7	91.8	1.000
Medications at hospital discharge			
Antiplatelets (%)	97.2	100.0	0.271
Beta-blockers (%)	50.0	52.6	0.847
Ca-antagonists (%)	13.9	9.3	0.526
Statins (%)	27.8	30.9	0.833
Diuretics (%)	47.2	41.2	0.559
Nitrates (%)	58.3	48.5	0.335

Data are shown as median or mean ± SD for continuous variables and percentages for dichotomous variables.
CK, creatine kinase; PCI, percutaneous coronary intervention; ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; HbA1c, glycated hemoglobin A1c.

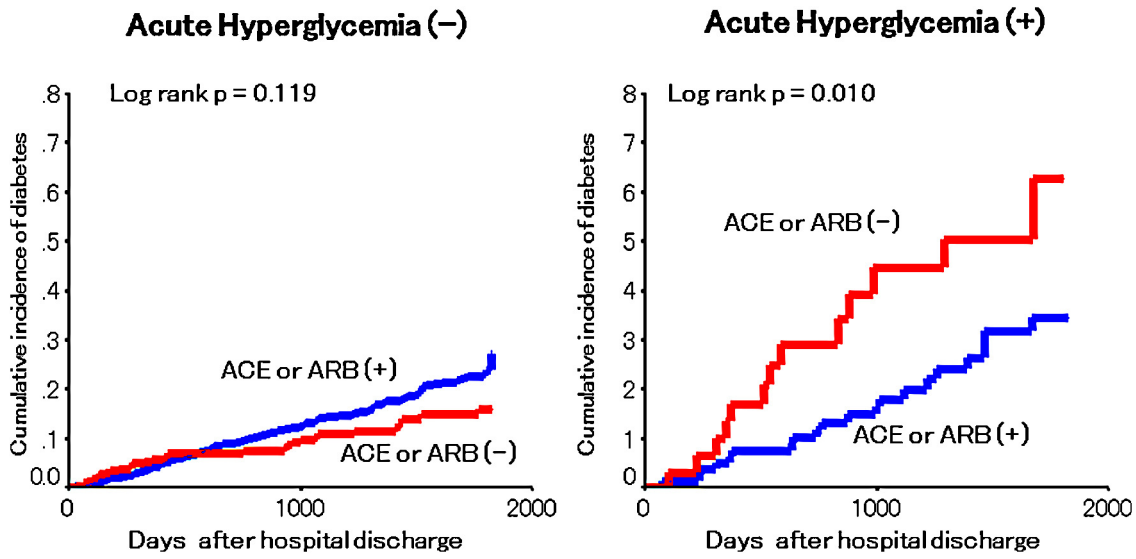

Fig. 3. Kaplan–Meier estimates for the development of *de novo* diabetes mellitus in acute myocardial infarction patients treated with and without renin–angiotensin system inhibitors based on to the prevalence of acute hyperglycemia. ACE, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker.

Table 5
Association between ACE inhibitors/ARBs and development of *de novo* diabetes mellitus.

	Development of *de novo* diabetes mellitus						
	Admission glucose < 200 mg/dl			Admission glucose ≥ 200 mg/dl			*p* for interaction
	Hazard ratio	95% CI	*p*-Value	Hazard ratio	95% CI	*p*-Value	
Univariate	1.359	0.923–2.000	0.120	0.411	0.203–0.829	0.013	
Multivariate							
Model 1	1.260	0.854–1.859	0.245	0.411	0.203–0.832	0.013	
Model 2	1.247	0.844–1.841	0.268	0.428	0.204–0.900	0.025	
Model 3	1.031	0.687–1.546	0.884	0.397	0.171–0.921	0.031	0.055

Model 1: adjusted for age and male gender; Model 2: adjusted for age, male gender, and HbA1c on admission; Model 3: adjusted for age, male gender, HbA1c on admission, history of hypertension, hyperlipidemia, smoking, and body mass index.
CI, confidence interval; ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; HbA1c, glycated hemoglobin A1c.

several possible explanations. First, the occurrence of AH in AMI patients without a history of DM might have reflected previously undiagnosed DM or preexisting impaired glucose tolerance. In the present study, to minimize these possibilities, we excluded patients with an admission HbA1c of >6.0%, regardless of their DM history. In addition, our analysis revealed that there was a stronger association between AH and the development of dn-DM in AMI patients with lower HbA1c levels (<5.6%) than those with higher HbA1c levels (≥5.6%). Because the interaction between HbA1c levels and AH was statistically significant (p value for interaction = 0.062), AH is considered to be particularly associated with the development of dn-DM in patients with lower HbA1c values. Thus, the observed relationship between dn-DM and stress-induced hyperglycemia in the post-AMI study patients was not likely a result of preexisting glucometabolic abnormalities, but was likely due to other mechanisms associated with AH. Furthermore, Ishihara et al. showed that 53% of the patients with admission glucose ≥11.1 mmol/L did not have DM in a study investigating the association between AH and results of glucose tolerance tests in AMI patients who had not been previously diagnosed as having DM [34]. Thus, although the presence of undiagnosed DM may be associated with AH in non-diabetic AMI patients, a positive association between AH and new onset of DM cannot be explained by only the presence of undiagnosed DM. Second, it is possible that sustained damage to glycometabolic systems might have resulted in the development of dn-DM in the post-AMI patients. Wallander et al. [35] suggested that early beta cell dysfunction and insulin resistance in AMI patients persisted up to 12 months after hospital discharge. In critical illness, the stress response is accompanied by the release of cortisol, catecholamines, glucagon, and growth hormone, which may induce continuous glucometabolic abnormalities [25–33]. Thus, in AMI patients with chronic heart failure, continuous release of cortisol, catecholamines, glucagon, and growth hormone might have induced glucometabolic abnormalities. Furthermore, proinflammatory cytokines, such as interleukin-1 and tumor necrosis factor alpha, cause hyperglycemia and peripheral insulin resistance by promoting similar hormones or by altering insulin receptor signaling [36,37]. On the other hand, it is well known that acute hyperglycemia or chronic heart failure increases oxidative stress. Evans et al. reported that oxidative stress plays a key role in causing insulin resistance and beta cell dysfunction [38]. Therefore, a continuous increase in oxidative stress might have induced sustained damage to glycometabolic systems, causing beta cell dysfunction or insulin resistance in AMI patients with chronic heart failure. Taken together, these lines of evidence suggest that sustained endocrine and metabolic changes might induce the development of dn-DM after AMI.

Another novel finding of the present study was that RAS inhibition was associated with reduced incidence of dn-DM in post-AMI patients with AH after survival discharge. Although the beneficial impacts of RAS inhibitors, such as ACE inhibitors and ARBs, on the prevention of new-onset type 2 DM have been reported in several clinical trials involving patients with hypertension, chronic heart failure, or stable coronary artery disease [39–41], data are limited in the secondary prevention setting after AMI. Thus, our present findings may provide important clinical information, as we found that treatment with RAS inhibitors at discharge was associated with a decreased incidence of dn-DM development in non-diabetic AMI patients with admission AH. It has been reported that angiotensin II increases hepatic glucose production and decreases insulin sensitivity, whereas ACE inhibitors and ARBs increase insulin sensitivity [42,43]. Therefore, the treatment of AMI patients with AH on admission using RAS inhibitors might have improved insulin sensitivity after AMI and decrease the incidence of dn-DM development. However, further investigations are warranted to examine the beneficial impacts and mechanisms of RAS inhibitors for reducing the incidence of dn-DM development after discharge in AMI patients presenting with AH.

Limitations

A few limitations of this study warrant mention. First, we did not have information regarding oral glucose tolerance tests (OGTT). Several studies have shown that abnormal glucose tolerance diagnosed by OGTT is common in AMI patients without a previous diagnosis of DM [9,44]. In the present study, we were not able to perform an OGTT to identify glucometabolic abnormalities in patients with AMI. Thus, it is possible that patients with undiagnosed DM were included in the study population. However, the impact of undiagnosed diabetic patients on the primary outcome was likely minimal, because the findings were unchanged when we employed an inclusion criterion of HbA1c levels on admission of 5.2% or lower, as this value reportedly excludes diabetic patients [45] (data not shown). Second, we did not have the data on the time elapsed from the last meal. The time elapsed from the last meal to blood collection likely affected plasma glucose levels. Third, this study was observational and was not randomized; thus, there may have been potential confounding factors, even after adjustment with baseline clinical and angiographic characteristics. However, our subjects may reflect the 'real world' population because they were typical, consecutively enrolled AMI patients hospitalized in an urban area of Japan.

Conclusions

The findings from the present study indicate that AH might not only be a marker of systemic stress induced by AMI, but also a predictor of the risk for dn-DM in non-diabetic AMI patients. Furthermore, we revealed that inhibition of the RAS may attenuate the risk of dn-DM in post-AMI patients with AH.

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