Original Article

Significant Association of Serum Adiponectin and Creatine Kinase-MB Levels in ST-Segment Elevation Myocardial Infarction

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Aims: Adiponectin, an adipocyte-specific secretory protein, abundantly exists in the blood stream while its concentration paradoxically decreases in obesity. Hypoadiponectinemia is one of risks of cardiovascular diseases. However, impact of serum adiponectin concentration on acute ischemic myocardial damages has not been fully clarified. The present study investigated the association of serum adiponectin and creatine kinase (CK)-MB levels in subjects with ST-segment elevation myocardial infarction (STEMI).

Methods: This study is a physician-initiated observational study and is also registered with the University Hospital Medical Information Network (Number: UMIN 000014418). Patients were admitted to Senri Critical Care Medical Center, given a diagnosis of STEMI, and treated by primary percutaneous coronary intervention (PCI). Finally, 49 patients were enrolled and the association of serum adiponectin, CK-MB, and clinical features were mainly analyzed.

Results: Serum adiponectin levels decreased rapidly and reached the bottom at 24 hours after recanalization. Such reduction of serum adiponectin was inversely correlated with the area under the curve (AUC) of serum CK-MB ($p=0.013$). Serum adiponectin concentrations were inversely correlated with AUC of serum CK-MB. In multivariate analysis, serum adiponectin concentration on admission ($p=0.002$) and collateral ($p=0.037$) were significantly and independently correlated with serum AUC of CK-MB.

Conclusion: Serum AUC of CK-MB in STEMI subjects was significantly associated with serum adiponectin concentration on admission and reduction of serum adiponectin levels from baseline to bottom. The present study may provide a possibility that serum adiponectin levels at acute phase are useful in the prediction for prognosis after PCI-treated STEMI subjects.

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Introduction

Adiponectin is characterized as an overabundance

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in the circulating blood stream and a paradoxical decrease in obesity despite an adipocyte-specific secretory protein[1-3]. Accumulating experimental evidence demonstrates the anti-atherosclerotic and anti-diabetic effects of adiponectin[4]. Adiponectin especially suppresses a series of progressive process of atherosclerosis, such as adhesion of monocytes to endothelial cells[5], proliferation of vascular smooth muscle cells[6], and foam cell formation of macrophages[7]. Interestingly, our recent immunohistochemical and immunoelec-

tron microscopic analyses showed that adiponectin protein was detected in endothelial cells in normal aorta, while it was observed not only in endothelial cells but also on the surface of synthetic smooth muscle cells and monocytes adherent to endothelial cells in atherosclerotic vasculature[8].

Importantly, increasing clinical evidences support the anti-atherosclerotic property of adiponectin. Low circulating adiponectin level (hypoadiponectinemia) should be one of the risks for atherosclerotic cardiovascular diseases[1-4]. Several clinical studies demonstrated the association of hypoadiponectinemia and ischemic heart diseases[9, 10]. Hypoadiponectinemia was also associated with coronary lesion complexity[11]. However, few reports have investigated the serial change in circulating adiponectin level in the acute phase of acute coronary syndrome (ACS). Kojima *et al.* demonstrated that adiponectin significantly decreased around 24–72 hours after hospitalization with acute myocardial infarction (AMI)[12].

Serum creatine kinase (CK)-MB has been clinically used for diagnosis of AMI and estimation of myocardial infarction size[13]. Peak CK-MB and the area under the curve (AUC) of serum CK-MB have been shown to predict mortality in subjects with primary percutaneous coronary intervention (PCI)-treated ST-segment elevation myocardial infarction (STEMI)[14-16]. However, the correlation between adiponectin and CK-MB has not been examined in patients with STEMI treated by primary PCI. The present study investigated the serial change of serum adiponectin level and the association of adiponectin and CK-MB in STEMI subjects who underwent primary PCI.

Methods

Subjects

The present study is an observational study titled "Study for correlation of organ injury with transition of adiponectin in acute and critical illness (RESPECT ALL)" and a physician-initiated, non-company sponsored single-center registry. Patients were admitted to Senri Critical Care Medical Center in Osaka Saiseikai Senri Hospital due to STEMI and treated by primary PCI from November 2013 to February 2015. After excluding 37 patients who were unable to sign the written informed consent or refused study participation, 9 patients who were transported under cardiac arrest, 2 patients who had previous old myocardial infarction, and 2 patients who were maintained by hemodialysis; 49 participants were enrolled and analyzed in the current study. The study protocol complied with the guidelines for epidemiologic studies

issued by the Ministry of Health, Labour, and Welfare of Japan was approved by the human ethics committees of Osaka Saiseikai Senri Hospital and Osaka University Hospital and was also registered with the University Hospital Medical Information Network (Number: UMIN 000014418).

All patients received the standard care available at the hospital, and no subject underwent any type of experimental intervention. Within 12 hours from the onset of chest pain, PCI was performed immediately after administration with 300 mg of clopidogrel and 200 mg of aspirin as the loading dose and intravenous injection of heparin at 8000 units, and a stent was successfully implanted in culprit lesion in most of patients by experienced interventionists. Thrombolysis in myocardial infarction (TIMI) flow grade at initial coronary angiography was evaluated as described previously[17]. Collateral flow was defined according to Rentrop classification[18]. After PCI, all patients received dual anti-platelet therapy (clopidogrel and aspirin), statins, and angiotensin-converting enzyme (ACE) inhibitors. Thrombectomy and intracoronary administration with vasodilators were left to the discretion of the interventional cardiologist.

Data Collection and Blood Sampling

The baseline data for the patients included age, sex, body mass index (BMI), coronary risk factors (diabetes mellitus, dyslipidemia, hypertension, and smoking habit), comorbidities (hyperuricemia, chronic kidney diseases, malignancy, cerebral infarction, chronic heart failure, and inflammatory diseases), previous medication, and time from onset to admission.

Blood samples for serum were allowed to coagulate at room temperature for 30 min, followed by centrifuged at 4000 rpm for 10 min, and stored at −80℃. Serum adiponectin concentration was measured by enzyme-linked immunosorbent assay (ELISA) (Otsuka Pharmaceutical Co., Ltd.). Serum CK-MB on admission and at 3, 6, 12, 24, 48, and 72 hours was measured by immunological inhibition method (Shino-Test Corporation, Beckman Coulter, Inc.). AUC of serum CK-MB was calculated as a sum of the trapezoid areas [a vertical axis: CK-MB (U/L), a horizontal axis: hour].

Statistical Analyses

Continuous variables, which were not normally distributed, were demonstrated as medians and interquartile ranges. Categorical variables were shown as counts and percentages. The Wilcoxon signed-rank test was used to compare continuous variables of % serum adiponectin concentration on admission and at 3, 6, 12, 24, 48, 72, and 168 hours. The Spearman's

rank correlation analysis was used to calculate correlation coefficient of parameters. The Jonckheere−Terpstra test was used to examine trend of AUC for CK-MB in each quartile group of serum adiponectin concentration on admission. The forced-entry logistic regression analysis was used to calculate the t-values of parameters. The significance level was set at $p < 0.05$. The software program SPSS Statistics 21 for Windows (IBM Japan, Tokyo) was used to analyze all data.

Results

Baseline Characteristics

The baseline clinical characteristics are shown in **Table 1**. The median age was 67 old and 69.4% of patients were men. The median BMI was 23.7 kg/m², indicating that study population was not obese subjects. As for coronary risk factors, prevalence of diabetes mellitus, dyslipidemia, hypertension, current smoker, and ex-smoker were 34.7%, 77.6%, 57.1%, 40.8%, and 22.4%, respectively. As for comorbidities, 20.4% of patients had hyperuricemia, and 16.3% of patients had renal insufficiency (eGFR < 60 ml/min/1.73 m²). No patient had a history of cerebral infarction, chronic heart failure, or inflammatory diseases. Among previous medications, the number of subjects treated with antihypertensive agents was relatively high, but that of patients treated with antidiabetic and/or lipid-lowering agents was low despite high frequency of diabetes and dyslipidemia.

Median time from onset of symptom to door was 88 minutes and the time of onset-to-recanalization was 124 minutes. As for culprit lesion of STEMI, 28.6% were right coronary artery (RCA), 2.0% was left main coronary artery (LMCA), 59.2% were left anterior descending coronary artery (LAD), and 10.2% were left circumflex coronary artery (LCx). Collateral arteries of Rentrop grade 1−3 were observed in 18.4% of patients. As for the initial TIMI flow grade, 83.7% were grade 0, 2.0% were grade 1, 10.2% were grade 2, and 4.1% were grade 3. As for stent use, drug-eluting stent (DES) was implanted in 87.7% of patients, bare metal stent (BMS) was used in 8.2% of patients, and no stent was used in 4.1% of patients. After primary PCI, complete and partial ST-segment resolutions were obtained in 44.9 % and 24.5 % of patients, respectively.

Change of Serum Adiponectin Concentrations

We first examined the sequential changes of serum adiponectin concentrations in patients with STEMI (**Fig. 1**). The % change of serum adiponectin concentration from baseline (on admission) was adopted since serum adiponectin levels were widely distributed. Interestingly, serum adiponectin levels decreased rapidly and reached the bottom at 24 hours after recanalization. They gradually and slowly increased from 24 to 168 hours (from Day 1 to Day 7). Compared to the baseline, the % changes of serum adiponectin concentration were 87.9 % [range: 82.7−97.1] ($p < 0.0001$) at 3 hours, 89.7 % [range: 83.6−96.8] ($p < 0.0001$) at 6 hours, 84.5 % [range: 78.3−93.8] ($p < 0.0001$) at 12 hours, 81.4 % [range: 74.0−87.6] ($p < 0.0001$) at 24 hours, 82.0 % [range: 73.6−95.0] ($p < 0.0001$) at 48 hours, 83.1 % [range: 75.2−92.0] ($p < 0.0001$) at 72 hours, and 85.3 % [range: 74.8−94.8] ($p < 0.001$) at 168 hours.

Correlations between Serum Adiponectin Concentration and Serum AUC of CK-MB

We next examined the correlation between serum adiponectin concentration and serum AUC of CK-MB, an indicator of myocardial damage[13]. As shown in **Fig. 2**, serum adiponectin concentrations were negatively correlated with serum AUC of CK-MB at baseline (on admission) ($r = -0.492$, $p < 0.001$; **Fig. 2A**), at 24 hours ($r = -0.459$, $p < 0.001$; **Fig. 2B**), and at 168 hours ($r = -0.474$, $p < 0.001$; **Fig. 2C**). The minimum values of serum adiponectin concentration (Min-adiponectin) were also inversely correlated with serum AUC of CK-MB ($r = -0.477$, $p < 0.001$; **Fig. 2D**).

Association between serum AUC of CK-MB and difference from baseline to Min-adiponectin [Δ adiponectin; (Min-adiponectin) − (baseline adiponectin)] was also analyzed as in **Fig. 3A**. Interestingly, serum AUC of CK-MB was inversely correlated with Δ adiponectin. ($r = -0.351$, $p = 0.013$).

Study population was divided into 4 groups in proportion to serum adiponectin level at baseline (Q1, 1.6−3.1 μg/mL; Q2, 4.3−6.1 μg/mL; Q3, 6.2−8.6 μg/mL; Q4, 9.2−26.5 μg/mL). **Fig. 3B** shows the association between serum AUC of CK-MB and each quartile. Subjects in the lowest baseline adiponectin group (Q1) showed the highest serum AUC of CK-MB. Serum AUC of CK-MB was significantly reduced from the highest quartile (Q1) to the lowest quartile (Q4) ($p < 0.001$ for trend).

Correlations between Serum AUC of CK-MB and Clinical Parameters

We finally investigated correlations between serum AUC of CK-MB and clinical parameters (**Table 2**). Serum adiponectin concentration at baseline (on admission) and age were negatively associated with serum AUC of CK-MB ($p < 0.001$ and $p = 0.006$, respectively). Male gender was positively associated with serum AUC of CK-MB ($p = 0.095$). To assess the determinants for serum AUC of CK-MB, the forced-

Table 1. Baseline characteristics

Age, years			67 (56, 75)
Male, % (n)			69.4 (34/49)
BMI, kg/m²			23.7 (22.1, 27.3)
Coronary Risk Factors	Diabetes Mellitus, % (n)		34.7 (17/49)
	Dyslipidemia, % (n)		77.6 (38/49)
	Hypertension, % (n)		57.1 (28/49)
	Smoking	Current smoker, % (n)	40.8 (20/49)
		Ex-smoker, % (n)	22.4 (11/49)
Comorbidities	Hyperuricemia, % (n)		20.4 (10/49)
	eGFR < 60, % (n)		16.3 (8/49)
	Malignancy, % (n)		4.1 (2/49)
	Cerebral infarction, % (n)		0.0 (0/49)
	Chronic heart failure, % (n)		0.0 (0/49)
	Inflammatory disease, % (n)		0.0 (0/49)
Medications	TZD, % (n)		0.0 (0/49)
	DPP4-I, % (n)		8.1 (4/49)
	Biguanide, % (n)		2.0 (1/49)
	Sulfonylurea, % (n)		4.1 (2/49)
	Insulin, % (n)		0.0 (0/49)
	Calcium channel blocker, % (n)		28.6 (14/49)
	ACE-I/ARB, % (n)		32.7 (16/49)
	Beta-blocker, % (n)		4.1 (2/49)
	Statin, % (n)		22.4 (11/49)
	Eicosapentaenoic acid, % (n)		0.0 (0/49)
	Fibrate, % (n)		0.0 (0/49)
	Antiplatelet drug, % (n)		4.1 (2/49)
Time	Onset to Door Time, min		88 (56, 190)
	Onset to Recanalization Time, min		124 (95, 270)
Culprit/Affected Vessel	RCA, % (n)		28.6 (14/49)
	LMCA, % (n)		2.0 (1/49)
	LAD, % (n)		59.2 (29/49)
	LCx, % (n)		10.2 (5/49)
Collateral, % (n)			18.4 (9/49)
Initial TIMI flow grade	0, % (n)		83.7 (41/49)
	1, % (n)		2.0 (1/49)
	2, % (n)		10.2 (5/49)
	3, % (n)		4.1 (2/49)
Stent	DES, % (n)		87.7 (43/49)
	BMS, % (n)		8.2 (4/49)
	None, % (n)		4.1 (2/49)
ST resolution	Complete, % (n)		44.9 (22/49)
	Partial, % (n)		24.5 (12/49)
	None, % (n)		30.6 (15/49)

Data are median and inter quartile ranges or percentage of subjects. BMI: body mass index, eGFR: estimated glomerular filtration rate, TZD: Thiazolidine derivative, DPP4-I: dipeptidyl peptidase-4 inhibitor, ACE-I: angiotensin converting enzyme inhibitor, ARB: angiotensin Ⅱ receptor blocker, RCA: right coronary artery, LMCA: left main coronary artery, LAD: left anterior descending coronary artery, LCx: left circumflex coronary artery, TIMI: thrombolysis in myocardial infarction trial, DES: drug eluting stent, BMS: bare metal stent.
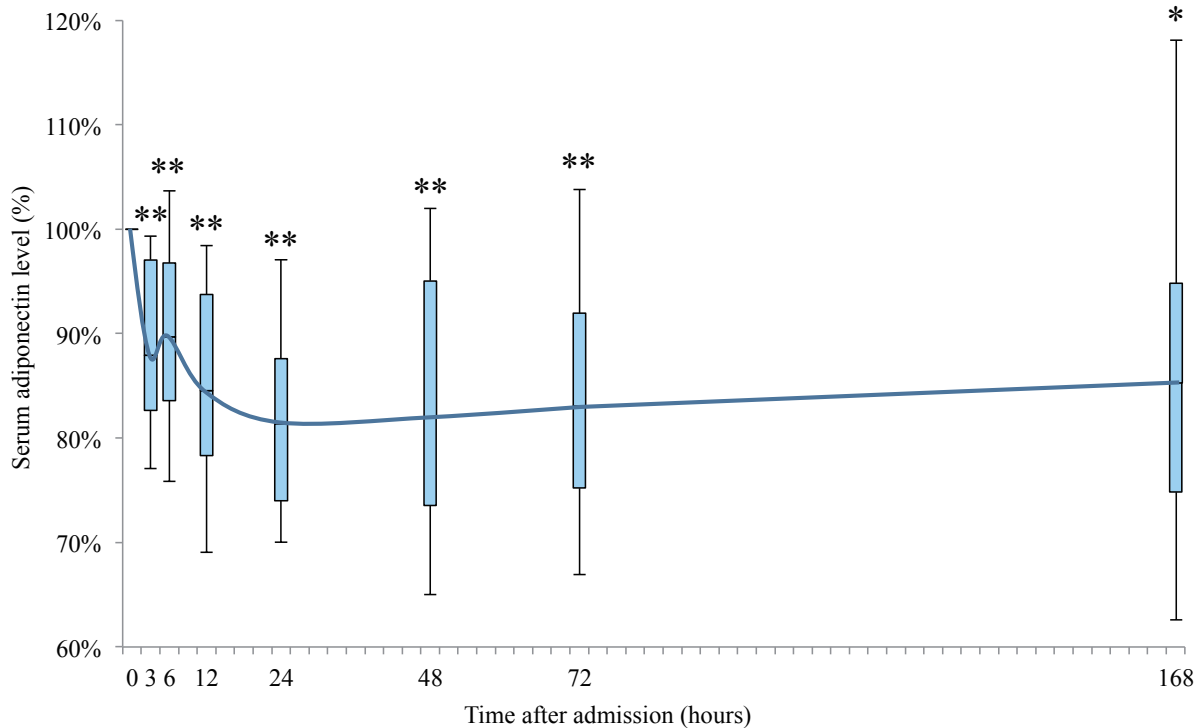
Fig. 1. Change of serum adiponectin levels.

Serum adiponectin concentration on admission was set at 100%. Curve shows the connected median, box shows the inter-quartile range, bar shows the 10th to 90th percentile of 49 patients. $*p < 0.001$, $**p < 0.0001$, compared with the 100% on admission

entry logistic regression analysis was performed including all clinical variables (Multivariate 1 in **Table 2**) or the confined variables relating to infarction size, such as culprit lesion, initial TIMI flow grade, collateral, and onset-to-recanalization time (Multivariate 2 in **Table 2**). Multivariate 1 demonstrated that serum adiponectin concentration on admission was significantly and independently correlated with serum AUC of CK-MB ($t = -2.086$, $p = 0.045$). In Multivariate 2, serum adiponectin concentration on admission ($t = -3.283$, $p = 0.002$) and collateral ($t = -2.149$, $p = 0.037$) were significantly and independently correlated with serum AUC of CK-MB.

Discussion

As shown in **Fig. 1**, serum adiponectin decreased from admission to 24 hours and gradually recovered to baseline after acute clinical phase. Such change of serum adiponectin was similar to previous studies in subjects with AMI ($n = 35$)[12] and LAD-based STEMI ($n = 98$)[19]. Similar to human subjects, such reduction of plasma adiponectin was also observed in myocardial ischemia-reperfusion (I-R) injury murine model[20, 21]. Interestingly, transient accumulation of the exoge-

nously administered adiponectin in heart tissue was shown in adiponectin knockout mice with myocardial I-R injury[20]. Our experimental reports demonstrated that adiponectin protein existed in the aorta[8, 22] and heart tissues[23], indicating that circulating adiponectin accumulates in cardiovascular tissues. We recently showed that T-cadherin is a critical player for tissue accumulation of adiponectin, for example, in T-cadherin knockout mice, adiponectin was not detected in cardiovasculature despite the 4- to 5-fold increase of circulating adiponectin[24]. In human subjects, we cannot examine the accumulation of adiponectin in injured tissues and/or vessels under ischemic condition, but a transient decline of serum adiponecitn may suggest the accumulation of adiponectin in injured tissues. The tissue accumulating adiponectin may exhibit a cardiovascular protective role. Importantly, as shown in **Fig. 3A**, a transient decline of serum adiponecitn was negatively correlated with serum AUC of CK-MB, indicating a possibility of abundant accumulation of adiponectin protected from myocardial damage and resulting in reduction of infarct size.

Animal models of myocardial infarction indicated that adiponectin protects against myocardial damage by enhancing AMP-activated protein kinase
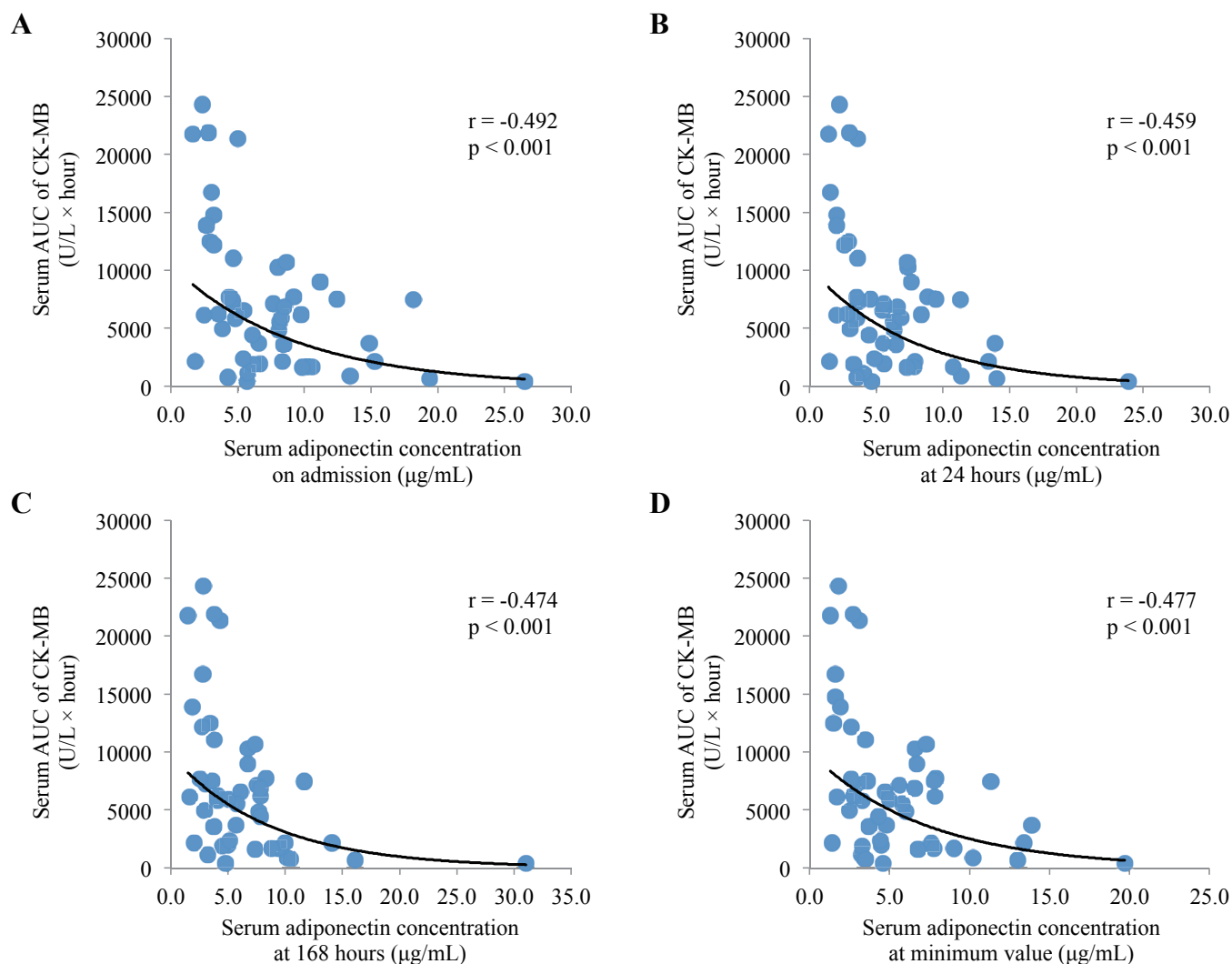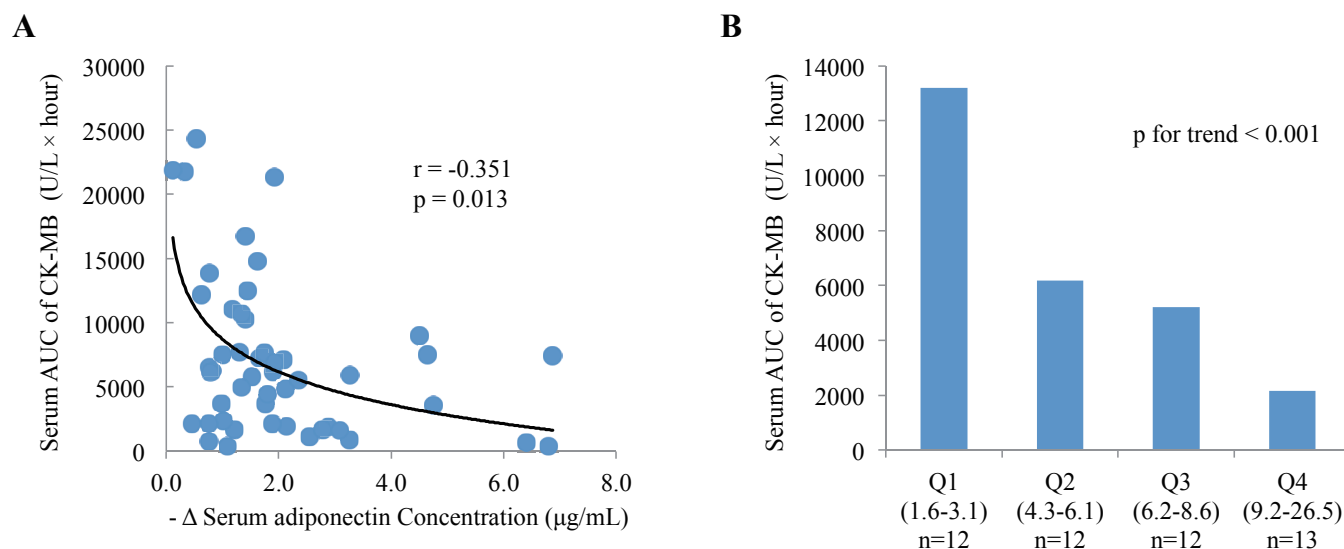
Fig. 2. Correlations between serum adiponectin concentration and AUC of CK-MB.

Serum adiponectin concentrations were shown in the horizontal axis, on admission (A), at 24 hours (B), at 168 hours (C), and at minimum value (D). CK-MB, MB fraction of creatine kinase; AUC, area under the curve

(AMPK) and cyclooxygenase (COX)-2 pathway and reducing oxidative stress[25, 26]. Interestingly, transplantation of scaffold-free induced adipocyte cell-sheet (iACS) derived from wild-type (WT) mice onto acute myocardial infarction heart significantly attenuated infarct size, left ventricular remodeling, and mortality compared to iACS from adiponectin knockout mice[27]. In addition, intracoronary administration of adiponectin reduced myocardial infarction size[28, 29]. These experimental data support our hypothesis that the abundant accumulation of adiponectin onto heart tissue protects from myocardial injury, which may result in a transient decline of serum adiponecitn during acute phase. Such hypothesis fits an inverse correlation between acute decrease of serum adiponectin and AUC of CK-MB. The impact of this acute change

of serum adiponectin level on cardiovascular events or mortality should be elucidated in future studies.

Currently, little is known about the relation between serum adiponectin level and myocardial infarction size. Shibata *et al* showed that serum adiponectin concentration was negatively correlated with infarct size measured by ^{123}I-BMIPP scintigraphy[30], while Alkofide H *et al.* demonstrated no association between log adiponectin and infarct size[31]. The present study is the first to demonstrate that serum adiponectin level on admission was one of inverse determinants in serum AUC of CK-MB (**Table 2**) for the first time. Determinants of myocardial infarction size have been shown, such as perfusion area of culprit coronary artery, time from onset to recanalization, collateral artery, initial TIMI grade flow, pre- and post-myocar-

A

r = -0.351
p = 0.013

B

p for trend < 0.001

Fig. 3. Impact of serum adiponectin on AUC of CK-MB.

A: Correlation between the reduction of serum adiponectin and serum AUC of CK-MB. Δ Serum adiponectin indicates the difference from baseline (on admission) to the minimum value of serum adiponectin (Min-adiponectin); Δ Serum adiponectin = (Min-adiponectin) − (baseline adiponectin). B: Serum AUC of CK-MB levels in quartile groups of serum adiponectin level on admission. Subjects were divided into 4 groups in proportion to serum adiponectin level at baseline (Q1, 1.6−3.1 μg/mL; Q2, 4.3−6.1 μg/mL; Q3, 6.2−8.6 μg/mL; Q4, 9.2−26.5 μg/mL). Shown are median values. Q1: minimum to the end of first quartile, Q2: the second quartile, Q3: the third quartile, Q4: the third quartile to maximum. CK-MB, MB fraction of creatine kinase; AUC, area under the curve

dial conditioning, and distal protection device. Similar to such factors, as previously demonstrated, collateral artery was also one of determinants in serum AUC of CK-MB in the present study. The existence of collateral was negatively correlated with serum AUC of CK-MB (**Table 2**), suggesting that collateral flows reduced infarct size. As shown in **Table 2**, the time from onset to recanalization was not a significant determinant, probably because its time in our hospital, Senri Critical Care Medical Center, was relatively shorter than in the other medical center (124 minutes in **Table 1**). All enrolled subjects were also treated with PCI using distal protection device. Medications, such as GⅡb/Ⅲa inhibitor, adenosine, and nitric oxide donors, were also demonstrated as determinants of myocardial infarction size[32]. There were no impacts of medication on myocardial infarction size in the present study, partly because all participants received ACE inhibitors, β-blockers, statins, and nicorandil after PCI. Administration of human atrial natriuretic peptide (hANP) reduced myocardial infarction size[33] and increased serum adiponectin level[34, 35], suggesting that hANP protects from myocardial damage partly through adiponectin. However, in the present study, there was no significant impact of hANP on serum AUC of CK-MB (**Table 2**), probably because the number of subjects treated with hANP was small (*n* = 16) and hANP was administered after recanaliza-tion.

Increasing evidence demonstrated the anti-atherosclerotic property of adiponectin. Pischon *et al.* clearly showed the significant association of hypoadiponectinemia and myocardial infarction in men in a large-scale, case-controlled study in the US[9]. Our previous cross-sectional study indicated that multivariate-adjusted odds ratios for coronary artery diseases (CAD) were 2.051 in subjects with hypoadiponectinemia (< 4.0 μg/mL) compared to subjects with normal adiponectin level (≥ 7.0 μg/mL)[10]. Hypoadiponectinemia was also associated with coronary lesion complexity[11]. As demonstrated in mouse models, adiponectin requires T-cadherin to exhibit its protective effects and accumulate cardiovascular system[24, 36, 37]. Interestingly, genome-wide association studies (GWAS) based on many independent cohorts demonstrated that genetic variation in CDH13 gene coding T-cadherin influences circulating adiponectin levels and cardiometabolic outcomes[38-44]. Collectively, T-cadherin-mediated accumulation of adiponectin onto the cardiovascular system may play a crucial role in cardiovascular events.

Several limitations of the present study should be considered. Serum adiponectin concentration is generally higher in women than in men[45]. Culprit lesions were different in individuals, and such a difference may impact on serum CK-MB levels. The present

Table 2. Correlations between parameters and serum AUC of CK-MB

Parameters	Serum AUC of CK-MB					
	Univariate		Multivariate 1		Multivariate 2	
	r	*p* value	*t* value	*p* value	*t* value	*p* value
Age	−0.385	0.006	−0.668	0.509		
Male	0.241	0.095	0.093	0.927		
BMI	0.205	0.159	0.447	0.636		
Diabetes Mellitus	0.188	0.196	−0.976	0.336		
Dyslipidemia	0.194	0.182	0.228	0.821		
Hypertension	−0.067	0.647	−0.059	0.954		
Smoking	0.054	0.711	−0.51	0.613		
LAD as affected vessel	0.22	0.128	1.189	0.243	1.125	0.267
Initial TIMI Flow	−0.181	0.214	−1.095	0.281	−1.237	0.223
Collateral	−0.153	0.295	−2.023	0.051	−2.149	0.037
Onset to Recanalization Time	0.064	0.663	−0.282	0.779	−0.276	0.784
ST resolution	−0.235	0.104	−0.247	0.807		
hANP administration	0.126	0.388	−0.439	0.663		
Serum adiponectin on admission	−0.492	<0.001	−2.086	0.045	−3.283	0.002

BMI: body mass index, LAD: left anterior descending coronary artery, TIMI: thrombolysis in myocardial infarction trial, hANP: human atrial natriuretic peptide

study used serum AUC of CK-MB as a surrogate marker of infarct size, but myocardial infarction area should be quantified by cardiac magnetic resonance imaging (MRI), RI myocardial scintigraphy, or left ventriculography (LVG). Serum adiponectin level may be altered by some medications, such as ACE inhibitors/angiotensin II receptor blockers (ACE-I/ARB), dipeptidyl peptidase-4 inhibitors (DPP4-I), and statins, but these effects on adiponectin levels are very little compared to that of thiazolidine derivative (TZD)[46-48]. Some statins were shown to increase serum adiponectin level as a pleiotropic effect[49, 50], but all subjects received statin therapy in the present study. Nine patients who were transported under cardiac arrest were excluded because CK-MB not always reflects infarct size in such a condition. Although the population size in this study was relatively small, we believe that it demonstrates a significant association between serum adiponectin and CK-MB levels in STEMI from real world data.

Conclusion

Herein, serum AUC of CK-MB in STEMI subjects treated by primary PCI was significantly associated with serum adiponectin concentration on admission and reduction of serum adiponectin levels from baseline to bottom. Data here may provide a possibility that serum adiponectin levels at acute phase are useful in the prediction for prognosis after PCI-treated

STEMI subjects, although further investigation will be needed in future.

Abbreviations

CK: creatine kinase; STEMI: ST-segment elevation myocardial infarction; PCI: percutaneous coronary intervention; AUC: area under the curve; CAD: coronary artery diseases; ACS: acute coronary syndrome; AMI: acute myocardial infarction; TIMI: Thrombolysis In Myocardial Infarction; ACE: angiotensin converting enzyme; BMI: body mass index; ELISA: enzyme-linked immunosorbent assay; RCA: right coronary artery; LMCA: left main coronary artery; LAD: left anterior descending coronary artery; LCx: left circumflex coronary artery; DES: drug eluting stent; BMS: bare metal stent; I-R: ischemia-reperfusion; AMPK: AMP-activated protein kinase; COX: cyclooxygenase; iACS: induced adipocyte cell-sheet; hANP: human atrial natriuretic peptide; RBP4: retinolbinding protein 4; TNF-α: tumor necrosis factor-α; MRI: magnetic resonance imaging; LVG: left ventriculography; ARB: angiotensin II receptor blockers; DPP4-I: dipeptidyl peptidase-4 inhibitors; TZD: thiazolidine derivative.

Authors' Contributions

T.N. acquired and analyzed data, and wrote the manuscript. N.M. conceived the study design, ana-

lyzed data, and wrote the manuscript. T.F., S.F., Y.F., H.N., S.F., M.Y., and H.N. participated in the discussion and the interpretation of data. H.S., Y.H., T.K., and I.S. participated in the discussion and the interpretation of data, and reviewed manuscript. All authors read and approved the final version of the manuscript.

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All authors declared no conflict of interests in present study.

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