Soluble Lectin-Like Oxidized Low-Density Lipoprotein Receptor-1 as an Early Biomarker for ST Elevation Myocardial Infarction

– Time-Dependent Comparison With Other Biomarkers –

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Background: The diagnostic sensitivity of myocardial necrosis markers, such as creatine kinase-MB (CK-MB), cardiac troponins, myoglobin and heart-type fatty acid-binding protein (H-FABP) for the earliest stage of ST-elevation myocardial infarction (STEMI), remains insufficient. We compared a new biomarker of plaque vulnerability (soluble lectin-like oxidized low-density lipoprotein receptor-1, sLOX-1) with other biomarkers at the earliest stage of STEMI.

Methods and Results: Plasma sLOX-1 levels were measured in 125 STEMI, 44 non-STEMI (NSTEMI) and 125 non-acute myocardial infarction (non-AMI) patients and were significantly ($P < 0.0001$) higher in the STEMI and NSTEMI than in the non-AMI patients (median, 25th and 75th percentiles: 241.0, 132.3 and 472.2 vs. 147.3, 92.9 and 262.4 vs. 64.3, 54.4 and 84.3 pg/ml, respectively). At the optimal cut-off value of 91.0 pg/ml, sLOX-1 discriminated STEMI from non-AMI with 89.6% sensitivity and 82.4% specificity. Time-dependent changes in sLOX-1, H-FABP, myoglobin, troponin T and CK-MB were analyzed in 27 STEMI patients. Elevated plasma sLOX-1 levels persisted for 24 h after admission, whereas other markers were not elevated at the time of admission and peaked at ≥ 2 h thereafter. The diagnostic sensitivity of sLOX-1, H-FABP, myoglobin, troponin T and CK-MB for STEMI upon admission (89 min after onset) was 93%, 78%, 70%, 56% and 33%, respectively.

Conclusions: Plasma sLOX-1 diagnosed the early stages of STEMI more accurately than H-FABP, myoglobin, troponin T and CK-MB. (*Circ J* 2011; **75**: 1433–1439)

Key Words: Diagnostic predictor; Ischemic injury; Myocardial necrosis; Plaque rupture

Although cardiovascular research and medicine are continuing to advance,¹ and the diagnosis and treatment of acute myocardial infarction (AMI) have significantly progressed over the past decade, AMI remains a major cause of mortality in developed countries.² Early re-opening of an infarct-related coronary artery using fibrinolysis or percutaneous coronary intervention (PCI) is the most important strategy for treating ST-elevation myocardial infarction (STEMI).^{3,4} Early diagnosis of STEMI is critical for successful implementation of the early-open-artery theory.^{4,5}

AMI is currently diagnosed using biomarkers of myocar-

dial damage, such as creatine kinase-MB (CK-MB),⁶ cardiac troponins,^{7–11} myoglobin¹² and heart-type fatty acid-binding protein (H-FABP),¹³ each of which has advantages and disadvantages.¹⁴ Although CK-MB and cardiac troponin^{15,16} are the previous and present gold standard markers, respectively, for myocardial necrosis, neither is an early marker of myocardial necrosis because they only start to elevate 3–4 h after the onset of AMI. On the other hand, although myoglobin and H-FABP are reported to be useful for the early detection of myocardial damage, their diagnostic specificity for AMI is insufficient.^{12,13}

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Plaque instability or rupture followed by thrombus formation precedes cardiac necrosis or ischemic injury in acute coronary syndrome (ACS).¹⁷ Thus, the identification of biomarkers that can detect plaque instability or rupture might enable earlier diagnosis of AMI. Lectin-like oxidized low-density lipoprotein (LDL) receptor-1 (LOX-1) is a receptor for atherogenic oxidized LDL in advanced human atherosclerotic plaques,¹⁸ and cleaved at the membrane-proximal extracellular domain by proteases into a soluble form.^{19,20} Thus, soluble LOX-1 (sLOX-1) is regarded as a marker of plaque rupture. In our previous studies, sensitive and specific immunoassays for human sLOX-1 revealed its diagnostic value for ACS at the earliest stage.^{19,21–23} Although sLOX-1 is considered to be a useful biomarker for the early diagnosis of ACS, including STEMI, its time-dependent diagnostic sensitivity for STEMI has not been compared to that of current biomarkers, namely CK-MB, troponin T, H-FABP and myoglobin.

Methods

We planned two studies to clarify the value of sLOX-1 for diagnosing STEMI and non-STEMI (NSTEMI) (Study-1), and the time-dependent changes of the sLOX-1 level in the early stages of STEMI (Study-2). The ethics committee of the hospital approved the study protocols, and written informed consent to participate in the investigations was given by all the study patients.

Study Population

Study-1 Between October 2007 and December 2009 at Nippon Medical School Chiba-Hokusoh Hospital we assigned consecutive 125 STEMI patients (111 males, 14 females; mean age: 64±12 years) and 44 NSTEMI patients (30 males, 14 females; mean age: 66±10 years) who arrived at the emergency room (ER) within 24h of the onset of chest symptoms and underwent coronary angiography (CAG). In addition, between October and December 2007 we assigned consecutive 125 patients (80 males, 45 females; mean age: 66±11 years) who underwent CAG without AMI (non-AMI group; 98 stable coronary artery disease (CAD) and 27 non-CAD) as the reference group.

Study-2 From October 2008 to February 2009 at Nippon Medical School Chiba-Hokusoh Hospital we enrolled 27 consecutive patients with STEMI (25 males, 2 females; mean age: 63±13 years) who arrived at the ER within 5h of the onset of chest symptoms and underwent CAG. We excluded the NSTEMI population from this study because there were many cases in which the exact time of onset was unclear because of the recurrent or ambiguous chest symptoms in the NSTEMI population.

In both studies, AMI was defined as prolonged chest pain (≥30 min) with the coronary artery lesion evidenced by CAG. STEMI and NSTEMI were respectively defined as AMI with and without ST segment elevation (≥0.2 mV) in at least 2 contiguous leads on ECG. Patients undergoing renal replacement therapy for acute or chronic kidney disease and those on a percutaneous cardiopulmonary support system for cardiogenic shock or fatal arrhythmia were excluded.

Measurement of sLOX-1 and Other Plasma Biomarkers

Sampling Methods Study-1: Peripheral blood samples

were obtained immediately before starting cardiac catheterization, and plasma separated by centrifugation was stored frozen at –80°C. Study-2: Peripheral blood samples were collected from the radial or femoral artery of each patient at the following time points: arrival at the ER (point 1), immediately before starting CAG (point 2), immediately after terminating PCI (point 3), at 6 (point 4), 12 (point 5) and 24 (point 6) hours after arrival at the ER and on discharge from the hospital (point 7).

Biomarker Measurements Plasma sLOX-1 levels were measured using a sandwich chemiluminescent enzyme immunoassay (CLEIA) with 2 newly developed anti-human LOX-1 monoclonal antibodies,²³ which was modified from the previously described enzyme-linked immunosorbent assay (ELISA) by use of the former polyclonal antibodies.²² CK-MB, troponin T, myoglobin and H-FABP were measured using a chemiluminescent enzyme immunoassay (ADVIA Centaur; Siemens Healthcare Diagnostics Inc, Tokyo, Japan), an electrochemiluminescence immunoassay (ECLusys Troponin TIII; Roche Diagnostics Co, Tokyo, Japan), a double antibody radioimmunoassay (Myoglobin Kit “Daichi” III; TFB Inc, Tokyo, Japan) and an enzyme-linked immunosorbent assay (Markit-M H-FABP; DS Pharma Biomedical Co Ltd, Osaka, Japan), respectively.

Statistical Analysis

Continuous variables are presented as mean±standard deviation and were compared using 1-way ANOVA test. Dichotomous variables were compared using χ^2 statistics. Because sLOX-1 levels and the time intervals did not distribute normally, these values are presented as median, and 25th and 75th percentiles and were compared between 2 groups by Mann-Whitney U test. Multivariable logistic regression analysis was applied to identify factors that were independently associated with AMI, by inclusion of factors that were significantly ($P<0.05$) associated with AMI in the univariable analysis. The optimal cut-off values of plasma sLOX-1 to diagnose STEMI and NSTEMI were calculated from a receiver-operating characteristic (ROC) curve generated from Study-1. The diagnostic sensitivity of the biomarkers for STEMI were calculated in Study-2 using this cut-off value of sLOX-1 and the known cut-off values of the other biomarkers at each sampling point. Data were statistically analyzed using the SPSS software package, version 16.0. A P -value <0.05 was considered statistically significant.

Results

Comparison of sLOX-1 Levels in STEMI, NSTEMI and Non-AMI Patients (Study-1)

The characteristics of the enrolled patients are shown in **Table 1**. Age, prevalence of risk factors, such as diabetes, hypertension, dyslipidemia, familial history of AMI and smoking, and serum creatinine levels were comparable among the STEMI, NSTEMI and non-AMI groups. Male sex and smokers were significantly more prevalent in the STEMI than in the NSTEMI and non-AMI groups; however, their prevalences were not significantly different between NSTEMI and non-AMI. Peak serum CK-MB levels were significantly higher in STEMI than in NSTEMI patients ($P<0.001$). The culprit vessels in AMI were comparable between STEMI and NSTEMI patients, except that left circumflex lesions were more prevalent in NSTEMI than in STEMI patients. The number of diseased vessels was comparable in both AMI groups. In addition, there was no significant cor-

Table 1. Characteristics of Patients in Study-1

	AMI		Non-AMI (n=125)	P value*
	STEMI (n=125)	NSTEMI (n=44)		
Male, n (%)	111 (89)**	14 (68)*	80 (64)**	<0.001
Age (years), mean $\pm$ SD	64 $\pm$ 12	66 $\pm$ 10	66 $\pm$ 11	0.430
Risk factors, n (%)				
Diabetes	45 (36)	11 (25)	37 (30)	0.327
Hypertension	75 (60)	34 (77)	87 (70)	0.074
Dyslipidemia	79 (63)	30 (68)	89 (71)	0.399
Familial history of AMI	24 (19)	11 (25)	37 (30)	0.160
Smoking	83 (66) ^{††}	21 (48) [†]	47 (38) ^{††}	<0.001
Creatinine (mg/dl), mean $\pm$ SD	0.90 $\pm$ 0.23	0.90 $\pm$ 0.48	0.92 $\pm$ 0.36	0.905
Peak CK-MB (IU/L), mean $\pm$ SD	177 $\pm$ 199	43 $\pm$ 94		<0.001
Culprit vessel, n (%)				
Right coronary artery	48 (38)	10 (23)		0.060
Left anterior descending artery	65 (52)	24 (55)		0.771
Left circumflex artery	12 (10)	10 (23)		0.026
No. of diseased vessels, mean $\pm$ SD	1.76 $\pm$ 0.81	1.71 $\pm$ 0.77		0.692

AMI, acute myocardial infarction; STEMI, ST elevation myocardial infarction; NSTEMI, non-ST elevation myocardial infarction; SD, standard deviation; CK, creatine kinase.

Continuous variables were compared by 1-way ANOVA and by Student's t-test, among STEMI, NSTEMI and non-AMI groups, and between STEMI and NSTEMI groups, respectively. Dichotomous variables were compared among 3 groups by χ^2 test.

*P=0.002 between STEMI and NSTEMI by χ^2 test; **P<0.001 between STEMI and non-AMI by χ^2 test; [†]P=0.029 between STEMI and NSTEMI by χ^2 test; ^{††}P<0.001 between STEMI and non-AMI by χ^2 test.

Figure 1. Comparison of plasma levels of soluble lectin-like oxidized low-density lipoprotein receptor-1 (sLOX-1) in patients with ST-elevation myocardial infarction (STEMI, n=125), non-ST-elevation myocardial infarction (NSTEMI, n=44) and non-acute myocardial infarction (non-AMI, n=125) among consecutive patients undergoing coronary angiography. Center horizontal lines indicate median values. Lower and upper edges of boxes indicate 25th and 75th percentiles, and lower and upper bars indicate 10th and 90th percentiles.

relation between plasma sLOX-1 and serum creatinine levels (P=0.203), indicating that renal function may not significantly affect plasma sLOX-1 levels. As shown in **Figure 1**, plasma levels of sLOX-1 were significantly higher in the STEMI (P<0.001) and NSTEMI (P<0.001) groups than in the non-AMI group. In STEMI patients, plasma sLOX-1 levels were sig-

Table 2. Comparison of sLOX-1 Levels in Patients With and Without Risk Factors

	n	sLOX-1 (pg/ml), mean $\pm$ SD	P value
Male	221	228.4 $\pm$ 269.7	<0.001
Female	73	145.6 $\pm$ 213.4	
Familial history of AMI, (+)	72	173.0 $\pm$ 225.1	0.054
Familial history of AMI, (–)	222	219.1 $\pm$ 268.8	
Hypertension, (+)	196	198.9 $\pm$ 246.5	0.370
Hypertension, (–)	98	225.8 $\pm$ 282.2	
Diabetes, (+)	93	205.6 $\pm$ 183.2	0.077
Diabetes, (–)	201	208.9 $\pm$ 288.0	
Dyslipidemia, (+)	198	210.4 $\pm$ 260.1	0.790
Dyslipidemia, (–)	96	202.6 $\pm$ 258.4	
Smoking, (+)	151	254.4 $\pm$ 287.4	<0.001
Smoking, (–)	143	158.6 $\pm$ 215.7	

sLOX-1, soluble lectin like oxidized low-density lipoprotein receptor-1. Other abbreviations see in Table 1.

nificantly more elevated than in NSTEMI patients (P=0.001). Median and 25th and 75th percentile values for STEMI, NSTEMI and non-AMI were 241.0, 132.3 and 472.2 vs. 147.3, 92.9 and 262.4 vs. 64.3, 54.4 and 84.3 pg/ml, respectively. In AMI patients, the number of diseased coronary vessels did not significantly affect plasma sLOX-1 levels; median sLOX-1 values for 1, 2 and 3 diseased vessels were 171.4, 214.1 and 245.7 pg/ml, respectively (P=0.466). In addition, plasma sLOX-1 levels correlated poorly with peak serum CK-MB levels (Spearman ρ =0.387, P<0.001). Plasma levels of sLOX-1 did not significantly differ between those with and without risk factors, such as a family history of AMI, hypertension, diabetes or dyslipidemia, except that sLOX-1 levels were significantly higher in males and smokers than in females and non-smokers (**Table 2**). Although males and smokers

Table 3. Multivariable Logistic Regression Analysis to Identify Factors Associated With AMI

	OR	95%CI	P value
sLOX-1	1.035	1.025–1.045	<0.001
Male	0.560	0.248–1.266	0.164
Smoking (+)	1.082	0.526–2.224	0.831

OR, odds ratio; CI, confidence interval. Other abbreviations see in Tables 1, 2.

were significantly more prevalent in the AMI group than in non-AMI and the sLOX-1 levels were significantly higher in males and smokers, multivariable logistic regression analysis to identify factors independently associated with AMI, including sLOX-1, sex and smoking, revealed that sLOX-1 alone was an independent factor associated with AMI (Table 3).

Defining the Optimal Cut-Off Value of sLOX-1 for STEMI (Study-1)

To obtain the optimal cut-off value of sLOX-1 to diagnose STEMI, plasma sLOX-1 levels were compared between the STEMI and non-AMI groups. The ROC curve of sLOX-1 for detecting STEMI using the non-AMI group as a negative reference (Figure 2A) indicated an area under the curve (AUC) value of 0.942. In addition, this ROC curve analysis revealed that sLOX-1 detected STEMI with 89.6% sensitivity and 82.4% specificity at an optimal cut-off value of 91.0 ng/ml. On the other hand, the ROC curve of sLOX-1 for detecting NSTEMI using the non-AMI group as a negative reference (Figure 2B) indicated an AUC value of 0.858, and sLOX-1 detected NSTEMI with 79.5% sensitivity and 82.4% specificity at an optimal cut-off value of 90.3 ng/ml, which was almost identical to the value for STEMI.

Comparison of Time-Dependent Changes in sLOX-1 With Other Biomarkers (Study-2)

The characteristics of the patients enrolled in the Study-2 are summarized in Table 4. The respective interval (median, 25th and 75th percentiles) from symptom onset to arrival at the ER (point 1) was 89, 66 and 173 min, to the start of CAG (point 2) was 142, 100 and 224 min and to the termination of PCI (point 3) was 230, 172 and 320 min. Sampling point 7 (discharge) was 16, 12 and 20 days after the onset of STEMI.

The time-dependent changes in sLOX-1, H-FABP, myoglobin, troponin T and CK-MB are shown in Figure 3. High plasma levels of sLOX-1 persisted for 24 h (point 6) after arrival at the ER (point 1), whereas H-FABP and myoglobin levels peaked at PCI termination (point 3) and then gradually decreased. Troponin T and CK-MB levels were highest at 6 h after ER arrival (point 4) and then gradually declined. The time-dependent changes in the sensitivity of each biomarker to diagnose STEMI are shown in Figure 4. The 91.0 pg/ml cut-off value of sLOX-1 was determined from the ROC curve in Study-1. The cut-off value for H-FABP, myoglobin, troponin T and CK-MB was 6.2, 60, 0.02 and 10.0 ng/ml, respectively, which are the standard cut-off values used to clinically diagnose STEMI in Japan. The sensitivity of sLOX-1 to diagnose STEMI upon arrival at the ER (point 1) was 93%, compared to 78%, 70%, 56% and 33%, for H-FABP, myoglobin, troponin T and CK-MB, respectively, indicating a higher diagnostic sensitivity of sLOX-1. These values were 100%, 93%, 89%, 70% and 48%, respectively, at the start of CAG (point 2), and 100%, 93%, 93%, 96% and 89%, respectively, at the termination of PCI (point 3). The diagnostic sensitivity of these biomarkers remained high (89–100%) at 12 h after arrival at the ER (point 5). At 24 h after ER arrival (point 6), the diagnostic sensitivity of sLOX-1, troponin T and CK-MB remained at 89%, 100% and 93%, respectively, whereas those of H-FABP and myoglobin fell to 56% and 67%, respectively.

Figure 2. Diagnostic sensitivity and specificity of soluble lectin-like oxidized low-density lipoprotein receptor-1 (sLOX-1) for ST-elevation myocardial infarction (STEMI) and non-STEMI (NSTEMI). Receiver-operating characteristic curves of sLOX-1 for diagnosis of STEMI (A) and NSTEMI (B) are shown. The area under the curve value for sLOX-1 was 0.942 for STEMI, and 0.858 for NSTEMI. Diagnostic sensitivity and specificity for STEMI were 89.6% and 82.4%, respectively, at a sLOX-1 cut-off value of 91.0 pg/ml. Diagnostic sensitivity and specificity for NSTEMI were 79.5% and 82.4%, respectively, at a sLOX-1 cut-off value of 90.3 pg/ml. AMI, acute myocardial infarction.

Table 4. Characteristics of Patients in Study-2

	n (%), mean $\pm$ SD or median (25–75th percentiles)
Male	25 (93)
Age (years)	63 $\pm$ 13
Risk factors	
Familial history of myocardial infarction	3 (11)
Hypertension	16 (59)
Diabetes	12 (44)
Dyslipidemia	20 (74)
Smoking	21 (78)
Time intervals (min)	
Time from the onset of STEMI to ER	89 (66–173)
Time from the onset of STEMI to start CAG	142 (100–224)
Time from the onset of STEMI to termination of PCI	230 (173–320)

ER, emergency room; CAG, coronary angiography; PCI, percutaneous coronary intervention. Other abbreviations see in Table 1.

Figure 3. Time-dependent changes in soluble lectin-like oxidized low-density lipoprotein receptor-1 (sLOX-1) (A), heart-type fatty acid-binding protein (H-FABP) (B), myoglobin (C), troponin T (D), and creatine kinase-MB (CK-MB) (E). Center horizontal lines indicate median values. Lower and upper edges of boxes indicate 25th and 75th percentiles, and lower and upper bars indicate 10th and 90th percentiles. Sampling points 1 (upon emergency room (ER) arrival), 2 (before starting coronary angiography) and 3 (after termination of percutaneous coronary intervention) were 89, 142 and 230 min (median) after ST-elevation myocardial infarction (STEMI) onset, respectively. Sampling points 4, 5 and 6 were 6, 12 and 24 h after arrival at ER, respectively. Sampling point 7 (at discharge from hospital) was 16 days (median) after the onset of STEMI.

Discussion

LOX-1, a receptor for atherogenic oxidized LDL,¹⁸ the expression of which is induced by factors related to atherogenesis and plaque vulnerability, such as proinflammatory cytokines,²⁴ angiotensin II,²⁵ high glucose²⁶ and oxidized LDL²⁷, is expressed on the surface of intimal smooth muscle cells²⁸

and lipid-laden macrophages^{28,29} in advanced human atherosclerotic plaques. LOX-1, furthermore, is cleaved at the membrane-proximal extracellular domain by proteases, including a disintegrin and metalloproteinase^{19,20} that may also be associated with plaque vulnerability or rupture, resulting in sLOX-1 release into the circulation.²⁰ In experimental animal models, LOX-1 expression is closely associated with morpho-

Figure 4. Time-dependent changes in the diagnostic sensitivity of the biomarkers for STEMI: sLOX-1 (A), H-FABP (B), myoglobin (C), troponin T (D), and CK-MB (E). The respective cut-off values were 91.0pg/ml, 6.2ng/ml, 60ng/ml, 0.02ng/ml and 10.0ng/ml. Abbreviations and sampling points are the same as those described in Figure 3.

logical plaque instability and cell apoptosis, as well as with the expression of matrix metalloproteinases and tissue factor, all of which are associated with plaque rupture and thrombus formation.^{30–32} Thus, proteases with enhanced activities in ruptured or rupture-prone vulnerable plaques may be responsible for the cleavage of LOX-1, which is abundantly expressed in advanced coronary atherosclerotic plaques. Taken together, these findings suggest that sLOX-1 is regarded as a biomarker of plaque rupture or plaque instability.

Because plaque instability or rupture precedes cardiac ischemia and necrosis in AMI, sLOX-1 release is expected to precede the release of biomarkers for myocardial injury or necrosis, such as CK-MB, cardiac troponins, myoglobin and H-FABP, in AMI. The results of the present study clearly demonstrate that plasma levels of sLOX-1 are useful for diagnosing AMI, especially the early stage. In this study, the plasma sLOX-1 level was elevated at the earliest stage (89 min from the symptom onset) of STEMI, which was earlier than the elevation of cardiomyocyte injury or damage markers such as troponin T, H-FABP, myoglobin and CK-MB, reflecting plaque rupture or instability. In addition, plasma sLOX-1 levels were higher in males and smokers than in females and non-smokers, probably because estrogen and smoking affect plaque vulnerability by protecting vascular cells from inflammation (the former)³³ and by inducing oxidative stress and inflammation (the latter).³⁴ According to our multivariable logistic regression analysis including sLOX-1, male sex and smokers in Study-1, sLOX-1 is an independent factor associated with AMI (Table 3). In the Study-1 subjects, both the sLOX-1 and peak CK-MB levels were higher in STEMI than in NSTEMI patients, and sLOX-1 levels poorly, but significantly, correlated with peak CK-MB levels, suggesting that the amount of vulnerable plaque burden may be poorly, but significantly, associated with myocardial infarct size. In Study-2, on the other hand, plasma sLOX-1 levels fell almost to the levels of the control subjects at 16 days (median) after

the onset of STEMI. These time-dependent reductions might result from the intensive treatment after hospitalization, including the pharmacological effects of statins, angiotensin-converting enzyme inhibitors, angiotensin-receptor blockers, and antiplatelet drugs.

The World Health Organization states that a clinical diagnosis of AMI is usually based on a history of chest pain, ECG changes and the elevation of cardiac-specific enzymes.³⁵ Although CK-MB is the gold standard for a diagnosis of AMI and we have extensive clinical experience, it is not a sensitive marker of increased myocardial necrosis.⁶ Many clinical studies during the 1990s clarified the values of troponins I and T for the diagnosis and risk stratification of AMI.^{7–11} Consequently, the European Society of Cardiology and the American College of Cardiology Committee jointly revised the definition of AMI,¹⁵ and cardiac troponins are listed as the biomarkers of preference in the latest definition,¹⁶ which states that AMI is the diagnosis when blood levels of cardiac biomarkers, preferably troponin I or T, are increased in the clinical setting of acute myocardial ischemia. However, the sensitivity of CK-MB and troponin (I or T) within 4 h of symptom onset (early stage of AMI) is low because they only start to elevate 3–4 h after onset. On the other hand, myoglobin and H-FABP serve as adjunct modalities for a diagnosis of early stage AMI because levels of these biomarkers begin to increase 1 h after onset.¹³ However, these biomarkers are not highly specific for a diagnosis of AMI, and combination with other modalities is recommended to diagnose the early stage of AMI.¹² We, therefore, speculate that the diagnostic sensitivity and specificity for AMI in the early stage would be improved by combination of biomarkers reflecting cardiomyocyte injury or damage and those for plaque rupture or vulnerability, including sLOX-1. It would be desirable if rapid measurement of blood sLOX-1 levels in the ER became commercially available in the future.

Conclusion

sLOX-1, a biomarker for plaque rupture or vulnerability, but not for myocardial damage, is more useful for diagnosing STEMI in the earliest stage than biomarkers of myocardial damage. However, the limitation of the present study would be the relatively small sample size, and thus the present findings should be confirmed by multicenter studies with larger sample sizes including NSTEMI patients. In addition, a recent pilot study has shown that sLOX-1 predicted prognosis, such as future recurrence of ACS or death, in ACS patients,³⁶ which also should be confirmed by large-scale prospective studies in the future.

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