Effects of mineralocorticoid receptor antagonist eplerenone on cardiac sympathetic nerve activity and left ventricular remodeling after reperfusion therapy in patients with first ST-segment elevation myocardial infarction

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Purpose. **The activation of the renin-angiotensin-aldosterone system prevents the uptake of norepinephrine and promotes structural remodeling of the heart. The mineralocorticoid receptor antagonist (MRA) eplerenone prevents left ventricular (LV) remodeling in patients with acute myocardial infarction, but its influence on cardiac sympathetic nerve activity (CSNA) has not been determined.**

Methods. **We retrospectively evaluated the first ST-segment elevation myocardial infarction (STEMI) patients in our database who underwent ^{123}I-metaiodobenzylguanidine (MIBG) scintigraphy 3 weeks after admission. Eighty-four STEMI patients after primary coronary angioplasty were selected, and used propensity score matching to compare patients who treated with MRA (N = 42), and those who did not (N = 42). The LV end-diastolic volume, end-systolic volume, and ejection fraction were determined by echocardiography, and plasma procollagen type III amino terminal peptide (PIIINP) was measured before and 3 weeks after treatment. The delayed total defect score (TDS), delayed heart/mediastinum count (H/M) ratio, and washout rate (WR) were determined using ^{123}I-MIBG scintigraphy after 3 weeks.**

Results. **Following primary angioplasty, age, gender, risk factors, culprit coronary artery, peak serum creatine phosphokinase concentration, and recanalization time were similar in the two groups. However, the MRA group showed significantly lower TDS and WR values (TDS: 22.8 ± 8.1 vs 32.2 ± 11.5, $P < 0.005$; WR: 31.1 ± 9.0% vs 42.7 ± 9.9%, $P < 0.001$) and a significantly higher H/M ratio (2.23 ± 0.41 vs 2.03 ± 0.36, $P < 0.05$) than the non-MRA group. The degree of change in LV parameters, and PIIINP were more favorable in the MRA group than in the non-MRA group. Moreover, multiple linear regression analyses revealed that both WR and not MRA treatment were significant predictor for LV remodeling, along with PIIINP concentrations.**

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Conclusion. **Administration of eplerenone improves CSNA and prevents LV remodeling in patients with a first STEMI. (J Nucl Cardiol 2022;29:2325–35.)**

Key Words: Myocardial infarction • sympathetic nervous system • scintigraphy • eplerenone

Abbreviations

ACE	Angiotensin-converting enzyme
ARB	Angiotensin receptor blocker
CSNA	Cardiac sympathetic nerve activity
EDV	End-diastolic volume
ESV	End-systolic volume
EPHESUS	Epleronone Post-acute myocardial infarction Heart failure Efficacy and SUrvival Study
H/M	Heart/mediastinum count
LV	Left ventricular
MIBG	Metaiodobenzylguanidine
MRA	Mineralocorticoid receptor antagonist
PCI	Percutaneous coronary intervention
PIIINP	Procollagen type III amino terminal peptide
RDS	Regional defect score
RDSI	Regional defect score index
STEMI	ST-segment elevation myocardial infarction
TDS	Total defect score
WR	Washout rate

See related editorial, pp. 2336–2339

INTRODUCTION

Since the Epleronone Post-acute myocardial infarction Heart failure Efficacy and SUrvival Study (EPHESUS)[1] reported the effectiveness of mineralocorticoid receptor antagonist (MRA) eplerenone in the treatment of acute myocardial infarction with left ventricular (LV) dysfunction, this agent has often been used in these patients. Aldosterone is well known to bind to mineralocorticoid receptors to regulate sodium and water reabsorption.[2] Moreover, aldosterone displays both myocardial and renal effects that can have profound implications for LV remodeling,[3] or abnormal cardiac sympathetic nerve activity (CSNA).[4] In the EPHESUS trial, the eplerenone was demonstrated to reduce mortality in patients with acute myocardial infarction,[1] and the beneficial outcome in the EPHESUS was shown to be associated with the suppression of cardiac collagen synthesis, and prevention of LV remodeling by this agent.[5]

Myocardial imaging with ^{123}I-metaiodobenzylguanidine (MIBG), an analog of norepinephrine, is useful for detecting abnormalities in the myocardial adrenergic nervous system in patients with acute myocardial infarction.[6] The myocardial ischemic area and cardiac ^{123}I-MIBG defect size are correlated in patients undergoing reperfusion therapy for these patients.[7] This imaging modality has been reported to be useful for predicting the adverse cardiac events in patients with ST-segment elevation myocardial infarction (STEMI).[8] Furthermore, previous studies reported that aldosterone inhibition normalizes autonomic neural control in failing human heart,[9] and attenuates enhanced CSNA in animal models of heart failure.[10] These favorable effects were associated with the increased myocardial uptake of norepinephrine mediated by aldosterone blockade.[4] Therefore, adding MRA to the standard therapy may normalize CSNA, i.e., improve ^{123}I-MIBG uptake in failing human heart. However, to our knowledge, no studies have examined the effects of eplerenone on CSNA evaluated by ^{123}I-MIBG scintigraphy in patients with STEMI.

Accordingly, we performed using our previously reported data,[8] to evaluate the hypothesis that mineralocorticoid receptor antagonist eplerenone improves CSNA in patients undergoing primary percutaneous coronary intervention (PCI) following their first STEMI.

MATERIALS AND METHODS

Patient Population

The consecutive patients admitted to our institution for STEMI were considered the study population. This study was sub-analysis using our previous database.[8] The diagnosis of STEMI was made on the basis of chest pain $>$ 30 minutes in duration, ST-segment elevation $>$ 2 mm in two electrocardiographic leads, and more than threefold increase in serum creatine phosphokinase activity. In the acute phase, all patients were treated in standard fashion, including primary PCI. Patients were excluded from the study if they had primary hepatic failure, severe renal failure, or active cancer. Moreover, patients with severe heart failure requiring mechanical support (mechanical ventilation, intraaortic balloon pumping, left ventricular assist device, or cardiac resynchronization therapy) and those requiring heart transplantation were excluded.[8] Patients treated with tricyclic antidepressant drugs, serotonin reuptake inhibitors, or other psychotropic medications as known to interfere with cardiac ^{123}I-MIBG scintigraphic findings[11] were also excluded.

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research

committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study.

Study Protocol

All patients underwent cardiac catheterization using the femoral and/or radial approach after an injection of 100 U·kg of heparin. The infarct-related artery was visualized using contrast injections. After confirmed occlusion of infarct-related vessel, all patients underwent PCI by standard techniques. All patients received oral anti-platelet agents. If necessary, patients were also started, and continued an oral angiotensin-converting enzyme (ACE) inhibitor, or an angiotensin receptor blocker (ARB), and/or a beta-adrenergic agent, as shown in Table 1. We measured the plasma concentration of procollagen type III amino terminal peptide (PIIINP) and performed echocardiography before primary PCI. A series of follow-up examinations (measurement of PIIINP concentrations and echocardiography) were repeated 3 weeks after angioplasty. We also performed ^{123}I-MIBG scintigraphy at the same time.

To evaluate whether the eplerenone treatment affected the CSNA in our STEMI patients, we retrospectively stratified our patients into MRA (N = 42), and non-MRA groups (N = 42), using propensity score matching.

Cardiac ^{123}I-MIBG Scintigraphy

The method used to conduct ^{123}I-MIBG imaging has been described previously.[12–14] ^{123}I-MIBG was obtained from a commercial source (FUJIFILM RI Pharma Co. Ltd., Tokyo, Japan). At 15 minutes and 4 hours after injection, anterior planar and SPECT images were obtained by the standard gamma camera (Millennium MPR, GE Medical Systems, Waukesha, Wisconsin).

Table 1. Clinical characteristics of patients in both groups

	MRA (N = 42)	Non-MRA (N = 42)	*P* value
Age (year)	67 ± 9	68 ± 9	0.571
Gender			0.801
Male	32 (76%)	31 (73%)	
Female	10 (24%)	11 (26%)	
Culprit coronary artery			
LAD	22 (53%)	21 (50%)	0.827
RCA	13 (31%)	16 (38%)	0.647
LCX	7 (16%)	5 (12%)	0.756
Current smoker	24 (57%)	23 (55%)	0.826
Diabetes mellitus	14 (33%)	16 (38%)	0.820
Dyslipidemia	31 (73%)	29 (69%)	0.810
Hypertension	30 (71%)	27 (64%)	0.641
Recanalization time (hr)	3.6 ± 1.6	3.9 ± 1.2	0.456
Stent implantation	41 (98%)	40 (95%)	0.966
Peak CPK (IU/L)	3302 ± 2207	3442 ± 2086	0.764
In-hospital medications			
ACE-inhibitor or ARB	37 (88%)	39 (93%)	0.713
Beta-blocker	36 (86%)	35 (83%)	0.763
Calcium antagonist	5 (26%)	4 (20%)	0.761
Diuretics	11 (23%)	10 (20%)	0.754
MRA (eprelenone)	42 (100%)	0 (0%)	-

Data are presented as the mean value SD or number (%).
MRA, mineralocorticoid receptor antagonist; *LAD*, left anterior descending coronary artery; *RCA*, right coronary artery; *LCX*, left circumflex coronary artery; *CPK* creatine phosphokinase; *ACE*, angiotensin-converting enzyme; *ARB*, angiotensin receptor blocker.

Global Analysis of ^{123}I-MIBG Scintigraphy

The heart/mediastinum count (H/M) ratio was determined from anterior planar delayed ^{123}I-MIBG images using the standard method. The washout rate (WR) was calculated as {([*H*]-[*M*])early − ([*H*]-[*M*])delayed}/([*H*]-[*M*])early × 100 (%), where [*H*] = mean count/pixel in the left ventricle and [*M*] = mean count/pixel in the upper mediastinum. In this study, time decay was not corrected for in the calculation of WR.

The delayed myocardial SPECT images of each patient were divided into the 17 segments recommended by the American Heart Association.[15] Tracer uptake in each segment was assessed semiquantitatively using visual scoring method with a 5-point scoring system (0 = normal uptake; 1 = mildly reduced uptake; 2 = moderately reduced uptake; 3 = significantly reduced uptake; 4 = no uptake). Total defect score (TDS) was calculated as the sum of all defect scores. Analysis was done in a blinded fashion by two independent observers with no knowledge of the clinical status or therapy of the subjects. The interobserver and intraobserver variability of defect scores were assessed by linear regression, and the levels of agreement were high (r = 0.90, P = 0.001 and r = 0.94, $P < 0.001$, respectively), as previously reported.[14]

Regional Analysis of ^{123}I-MIBG Imaging

To evaluate regional adrenergic dysfunction in patients with STEMI on SPECT images, we calculated a regional defect score (RDS) for each of the 17 segments. Then the infarcted RDS index (RDSI) was calculated as the average RDS of the culprit segments. The non-infarcted RDSI was also calculated as the average RDS of the non-culprit segments, as previously reported.[8]

Echocardiography

Echocardiography was performed using standard methods in a blinded manner, before and 3 weeks after angioplasty. The LV end-diastolic volume (EDV), end-systolic volume (ESV), and ejection fraction were calculated using the 2D-biplane method.[16]

Plasma PIIINP Concentrations

Blood samples were collected from an antecubital vein. The PIIINP plasma levels were measured by a specific immunoradiometric assay using a commercial kit (CIS, Bio, International, Nagoya, Japan), as previously reported.[17,18]

Statistical Analysis

The analyses were performed using SPSS version 25 (IBM Corp, Chicago, IL), or SAS version 9.4 (SAS Institute Inc., Cary, NC). Numerical results were expressed as the mean ± SD. In all the analyses, $P < 0.05$ was considered statistically significant. A propensity-matched analysis was conducted to minimize the selection bias for eplerenone administration.[19] To obtain the propensity score for the probability that eplerenone would be administered, multivariate logistic regression analyses were conducted. The propensity score was based on the following variables: age, sex, smoking, culprit coronary artery, peak serum creatine phosphokinase concentration, and the presence of dyslipidemia, diabetes, and hypertension. Patients in the MRA and non-MRA groups were matched one to one to an accuracy of two digits, using the estimated propensity score for treatment with or without oral eplerenone. In our database, 42 patients were treated with eplerenone, thus 42 matched patients were extracted from the non-MRA group.

Categorical data were compared between the 2 groups using 2-sided chi-square tests, and differences between continuous variables were evaluated using the unpaired *t*-test. Deviations from the group baseline were evaluated using a paired *t*-test, and between the 2 groups using 2-way ANOVA. Relationship between degree of changes in PIIINP and left ventricular volume were assessed using linear regression analysis. To determine the contribution of LV remodeling, the variables of interest were examined by univariate and stepwise multiple analyses, using degree of change in LVEDV, and LVESV (delta-LVEDV, and delta-LVESV, respectively).

RESULTS

Clinical Characteristics

No significant differences were observed in the clinical characteristics or cardiac medications were found between the two groups. Age, gender, culprit coronary artery, risk factors, recanalization time, and peak creatine phosphokinase concentrations in the acute phase were similar for both groups (Table 1). No differences were observed in the in-hospital medications (except eplerenone) and clinical follow-up of the two study groups. There were no differences in medication dose (all, P = NS), and duration (all, P = NS) between the two groups.

Comparison of LV Parameters at Baseline and 3 Weeks After Treatment

The LV ejection fraction, end-diastolic volumes, and end-systolic volumes, are shown in Figure 1. In the MRA group, LV end-diastolic and end-systolic volumes did not change significantly after 3 weeks of treatment. However, LV ejection fraction was significantly increased after 3 weeks of treatment ($P < 0.01$). By contrast, in the non-MRA group, the LV end-diastolic volume was significantly increased after 3 weeks ($P < 0.05$). Moreover, the degree of change in LV ejection fraction in the MRA group was significantly higher ($P < 0.01$), and that in LV end-systolic volume was significantly lower ($P < 0.05$) than in the non-MRA group.

Comparison of Cardiac ^{123}I-MIBG Scintigraphic Findings 3 Weeks After Treatment

The TDS, H/M ratio, and WR are shown in Table 2 and Figure 2. The TDS in the MRA group was significantly lower than in the non-MRA group ($P < 0.005$). The H/M ratio in the MRA group was significantly higher than in the non-MRA group ($P < 0.05$). Finally, the WR in the MRA group was significantly lower than in the non-MRA group ($P < 0.001$).

Table 2 provides a summary of infarcted RDSI and non-infarcted RDSI. The infarcted RDSI in the MRA group was significantly lower than in the non-MRA group ($P < 0.005$). Finally, non-infarcted RDSI was also significantly lower than in the non-MRA group ($P < 0.001$).

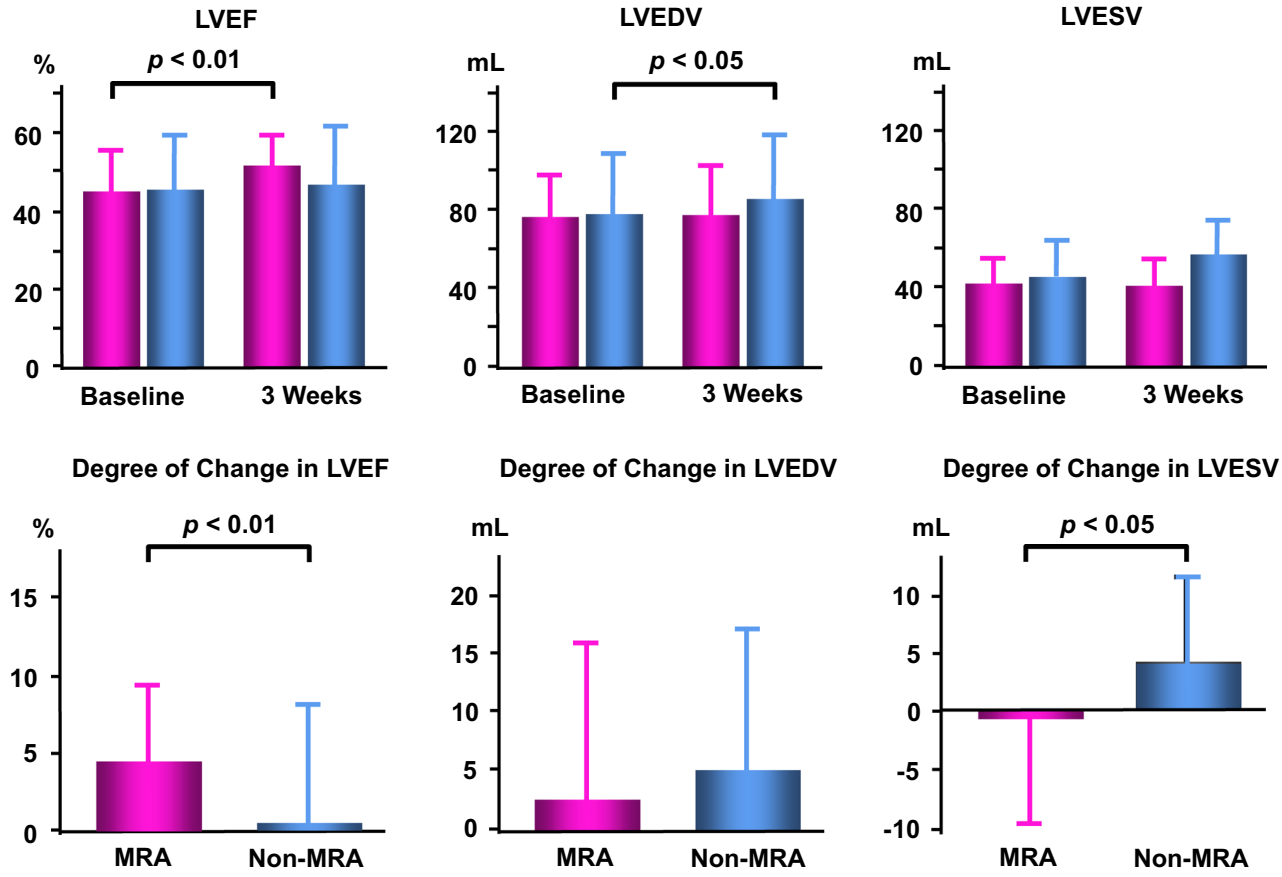

Figure 1. Changes in the LVEF, LVEDV, and LVESV in the two groups from baseline to three weeks after treatment (Top). The degree of changes (value at 3 weeks minus baseline) in the LVEF, LVEDV, and LVESV (Bottom). Pink bars indicate the MRA group, and the sky blue bars indicate the non-MRA group. *LV*, left ventricular; *EF* ejection fraction; *EDV*, end-diastolic volume; *ESV*, end-systolic volume; *MRA*, mineralocorticoid receptor antagonist.

Table 2. MIBG scintigraphic parameters of patients in both groups

	MRA (N = 42)	Non-MRA (N=42)	*P* value
Global analysis			
TDS	22.8 ± 8.1	32.2 ± 11.5	< 0.005
H/M ratio	2.23 ± 0.41	2.03 ± 0.36	< 0.05
WR	31.1 ± 9.0	42.7 ± 9.9	< 0.001
Regional analysis			
Infarcted RDSI	2.7 ± 0.7	3.3 ± 0.8	< 0.005
Non-infarcted RDSI	0.6 ± 0.4	1.2 ± 0.7	< 0.001

Data are presented as the mean value ± SD.
TDS, total defect score; *H/M*, heart/mediastinum count; *WR*, washout rate; *RDSI* regional defect score index.

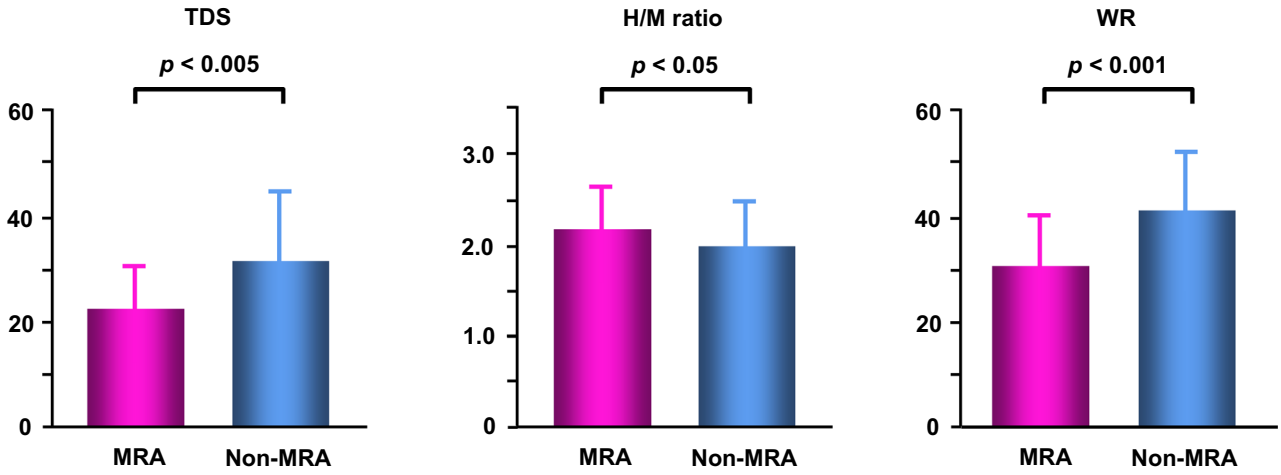

Figure 2. Comparison of cardiac ^{123}I-metaiodobenzylguanidine scintigraphic findings three weeks after treatment for TDS, H/M ratio, and WR in the 2 groups. Pink bars indicate the MRA group, and the sky blue bars indicate the non-MRA group. *TDS*, total defect score; *H/M* heart/mediastinum count; *WR* washout rate.

Comparison of PIIINP Concentrations at Baseline and 3 Weeks After Treatment

PIIINP concentrations are shown in Figure 3. In both groups, the plasma PIIINP concentrations were significantly increased after 3 weeks of treatment ($P < 0.01$ in the MRA group and $P < 0.001$ in the non-MRA group). However, the change in PIIINP in the MRA group was significantly lower than that observed in the non-MRA group ($P < 0.005$).

Relationship Between Degree of Changes in PIIINP and Left Ventricular Volume Baseline and 3 Weeks After Treatment

There were significant correlations between the degree of change in PIIINP concentration and that in LVEDV ($r = 0.628$, $P < 0.001$), or LVESV ($r = 0.616$, $P < 0.001$) in the MRA group (Figure 4). In contrast, there were no relationships between these parameters in the non-MRA group (LVEDV; $r = 0.219$, $P = 0.163$, LVSDV; $r = 0.232$, $P = 0.139$).

Evaluation of Factors Predicting Increased Left Ventricular Volume

Table 3 shows the results of the univariate and stepwise multiple linear regression model analyses assessing factors that predict an increase in LV volumes. In the linear regression of LVEDV, univariate analysis indicated that not being treated with ACE-inhibitor or ARB, alongside MRA, PIIINP concentrations, and WR were predictive factors. Stepwise multiple linear

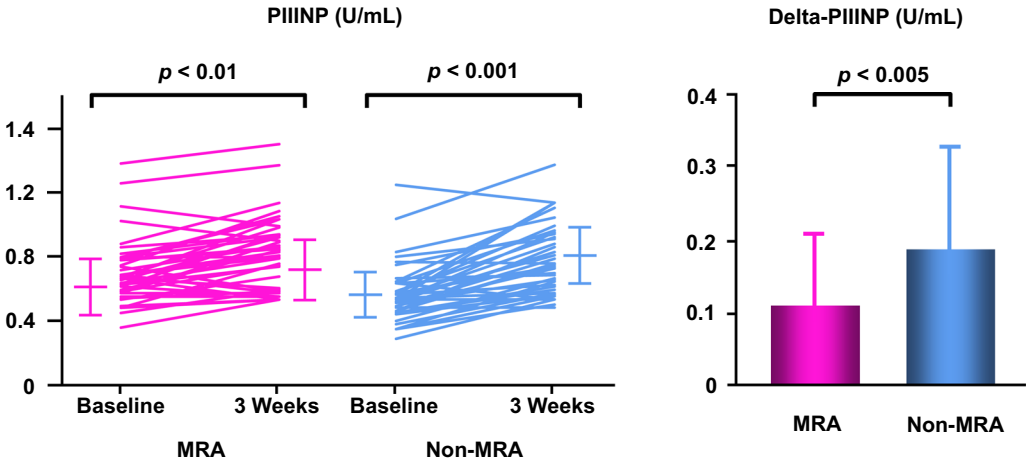

Figure 3. Changes in PIIINP concentrations from baseline to three weeks after treatment (left side) and the degree of change in PIIINP concentrations (right side). Pink bars indicate the MRA group, and the sky blue bars indicate the non-MRA group. *PIIINP*, procollagen type III aminoterminal peptide.

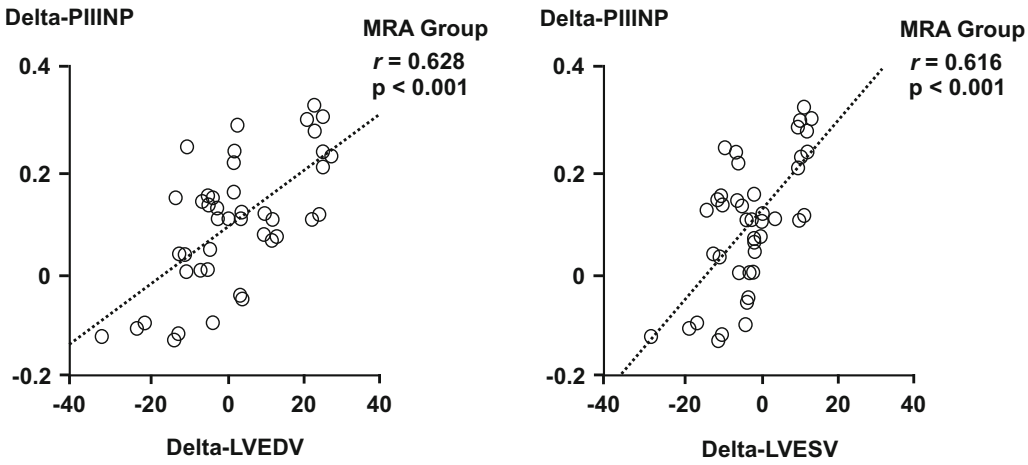

Figure 4. Correlation between the degree of change in PIIINP concentrations and that in LVEDV (left side), or LVESV (right side) from baseline to three weeks after MRA treatment. *PIIINP*, procollagen type III aminoterminal peptide; *LV*, left ventricular; *EDV*, end-diastolic volume; *ESV*, end-systolic volume; *MRA*, mineralocorticoid receptor antagonist.

regression model analysis also showed that WR was most significant predictor for increasing LVEDV, along with not MRA treatment, and PIIINP concentrations.

In the linear regression of LVESV, univariate analysis indicated that the peak CPK, not being treated with MRA, PIIINP concentrations, and WR were predictive factors. Stepwise multiple linear regression model analysis also showed that WR was most significant predictor for increasing LVESV, along with not MRA treatment, and PIIINP concentrations.

DISCUSSION

The findings of this study demonstrate for the first time that the addition of eplerenone to standard therapy can improve CSNA and prevent LV remodeling in patients with a first STEMI, as compared to standard conventional therapy alone. This agent can also suppress cardiac collagen synthesis during the acute to subacute phase of STEMI, following primary PCI.

Aldosterone promotes retention of sodium, loss of magnesium and potassium, myocardial and vascular

Table 3. Univariate and multivariate linear model of delta -LVEDV and delta -LVESV

	Univariate Correlation coefficient	*P* value	Multivariate Beta-coefficient	*P* value
Linear regression analysis of delta-LVEDV				
Age	0.007	0.949		
Gender (male = 1)	0.188	0.087		
LAD (yes = 1)	0.201	0.067		
Diabetes mellitus	0.020	0.845		
Peak CPK (IU·L)	0.164	0.137		
ACE-inhibitor or ARB	− 0.272	0.012	− 0.160	0.139
Beta-blocker	− 0.161	0.145		
MRA (eprelenone)	− 0.360	0.001	− 0.205	0.037
PIIINP	0.286	0.008	0.259	0.011
WR	0.411	< 0.001	0.374	0.001
Linear regression analysis of delta-LVESV				
Age	0.012	0.914		
Gender (male = 1)	0.118	0.284		
LAD (yes = 1)	0.284	0.121		
Diabetes mellitus	0.054	0.626		
Peak CPK (IU·L)	0.323	0.015	0.156	0.188
ACE-inhibitor or ARB	− 0.213	0.052		
Beta-blocker	− 0.185	0.155		
MRA (eprelenone)	− 0.344	0.006	− 0.305	0.009
PIIINP	0.289	0.012	0.287	0.011
WR	0.369	0.001	0.318	0.003

LVSDV, left ventricular end-systolic volume; *LVEF*, left ventricular ejection fraction; *LAD*, left anterior descending coronary artery; *CPK*, creatine phosphokinase; *ACE*, angiotensin-converting enzyme; *ARB*, angiotensin receptor blocker; *MRA*, mineralocorticoid receptor antagonist; *PIIINP*, plasma procollagen type III amino terminal peptide; *WR*, washout rate.

fibrosis,[3] baroreceptor dysfunction,[20] vascular damage and arterial noncompliance,[21] structural remodeling, sympathetic activation, and parasympathetic inhibition.[9,10] Moreover, Yoshimura et al.[22] reported that the aldosterone synthase gene is expressed in cardiac tissue, and in another report, they concluded that aldosterone is produced in the ventricles of the failing human heart.[23] The same group has also demonstrated that aldosterone induces the expression of ACE messenger RNA in cultured neonatal cardiocytes.[24] Therefore, eplerenone may have cardioprotective effects by directly suppressing aldosterone production in the cardiac tissue of failing heart.

^{123}I-MIBG, an analogue of the adrenergic-neuron-blocking agent guanethidine, is thought to utilize the same mechanism of myocardial uptake and release as norepinephrine.[25] An association between myocardial norepinephrine concentrations by the radioenzymatic method and myocardial ^{123}I-MIBG uptake in heart failure patients has been reported previously.[26] Therefore, cardiac ^{123}I-MIBG imaging may be a useful tool for detecting abnormalities of the myocardial adrenergic nervous system in patients with acute myocardial infarction.[6,7] We and other investigators reported that the cardioprotective treatments with ACE inhibitors,[27,28] ARBs,[12,29] beta-blockers,[14,28] or spironolactone[30,31] can improve CSNA, on the basis of cardiac ^{123}I-MIBG scintigraphic findings. However, there are no reports on the changes in cardiac ^{123}I-MIBG scintigraphic findings in response to eplerenone administration in patients with STEMI. In this study, the TDS, H/M ratio, and WR determined by cardiac ^{123}I-MIBG scintigraphy were favorable in the eplerenone group compared to the non-eplerenone group.

On the other hand, we previously reported that ^{123}I-MIBG scintigraphic parameters three weeks after the onset of STEMI provide useful predictors of cardiac events in patients with STEMI.[8] In that report, we concluded that the WR was a powerful predictor of both cardiac death and major adverse cardiac events in 213 patients with STEMI. As a result, throughout the years, we have focused on the pharmacological improvement

of CSNA. This study found that adding eplerenone to standard therapy had beneficial effects on ^{123}I-MIBG scintigraphic findings, as compared with standard treatment alone. Therefore, our findings demonstrate for the first time that eplerenone therapy, in other words, aldosterone blockade had beneficial effects on the CSNA in patients with STEMI, indicating that this may improve patient outcomes, as shown previous study.[1]

It is known that regional sympathetic denervation is associated with contractile dysfunction and myocardial fibrosis in patients with heart failure.[32] Moreover, very interestingly, Kramer et al.[33] reported that increased sympathetic denervation in adjacent non-infarcted regions evaluated by ^{123}I-MIBG scintigraphy leads to LV remodeling after acute myocardial infarction. In this study, both infarcted and non-infarcted RDSI in the eplerenone group were significantly lower than those in the non-eplerenone group. We suggest that adding eplerenone to standard therapy not only improves CSNA, but also attenuates myocardial fibrosis and prevents LV remodeling, as compared with standard conventional therapy following reperfusion in patients with STEMI.

Plasma PIIINP concentrations may constitute a biochemical marker for myocardial fibrosis or LV remodeling in patients with failing heart.[34,35] Klappacher et al.[34] reported the significant positive correlation between plasma PIIINP and the amount of myocardial collagen type III on cardiac biopsy specimens of heart failure patients. Moreover, Host et al.[35] showed that the plasma PIIINP was higher in those patients with a poor prognosis after myocardial infarction. We have previously reported the association between plasma PIIINP concentrations and ^{123}I-MIBG scintigraphic parameters after medical treatments in STEMI patients.[17,18] In the present study, the plasma PIIINP concentrations in the acute phase were significantly increased after 3 weeks in both groups. However, the degree of change in PIIINP was significantly lower in the eplerenone group than in the non-eplerenone group.

Moreover, increasing of LV volume (i.e., progression of LV remodeling) has been shown to be associated with the poor prognosis in patients with myocardial infarction.[36] Therefore, increasing effort has been directed toward pharmacological attenuation of LV volume after myocardial infarction. Hayashi et al.[37] reported the favorable effect in LV volumes in patients with acute myocardial infarction after MRA treatment compared with standard conventional treatment. Similarly, in this study, degree of changes in LV volume after the 3 weeks treatment in the eplerenone group were favorable compared with the non-eplerenone group. Furthermore, both this treatment and WR evaluated by ^{123}I-MIBG scintigraphy decrease LV volume after primary coronary angioplasty in STEMI patients, and this finding was confirmed by multiple linear regression analysis. Our findings indicate that eplerenone treatment leads to improved CSNA and results in LV remodeling after primary coronary angioplasty, and therefore ^{123}I-MIBG scintigraphy may help guide the use of eplerenone.

Study Limitations

The small number of patients with STEMI included in this study was a limitation. Moreover, ^{123}I-MIBG scintigraphic parameters of our patients were better compared with previous major study of failing human heart.[38] Since the H/M ratio in the MRA group and non-MRA group were relatively high, these values were classified as low-risk groups from previous study.[38] However, because the cut-off value of the H/M ratio in our database was 1.85,[8] suggesting that the difference between patients with and without MRA treatment would be useful. Therefore, in the future, we need to evaluate the effects of MRA for predicting the prognosis in the large number of patients including severe cases in myocardial infarction.

NEW KNOWLEDGE GAINED

While it is known that the cardioprotective treatments can improve CSNA evaluated by ^{123}I-MIBG scintigraphy in patients with STEMI, we have shown that MRA have similar effects. Therefore, MRA treatment may be effective for reducing the incidence of cardiac events for these patients.

CONCLUSION

The TDS, H/M ratio, and WR determined by cardiac ^{123}I-MIBG scintigraphy were better by use of eplerenone, as compared with the standard conventional therapy. Three weeks after treatment, LV parameters in the eplerenone group more favorable than those in the conventional therapy group. These findings indicate that administration of eplerenone can improve CSNA and prevent LV remodeling in patients with a first STEMI.

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