Doctoral Thesis in
Medical Sciences

Prognostic Impact of Left Ventricular Mass Change in Patients with ST-elevation Myocardial Infarction

Ajou University Graduate School

Medical Sciences Major

Jin-Sun Park

Prognostic Impact of Left Ventricular Mass Change in Patients with ST-elevation Myocardial Infarction

Seung-Jea Tahk, M.D., Ph.D., Advisor

I submit this thesis as the

Doctoral thesis in Medical Sciences.

February 2018

Ajou University Graduate School

Medical Sciences Major

Jin-Sun Park

This certifies that the dissertation of

Jin-Sun Park is approved.

SUPERVISORY COMMITTEE

_____

Myeong-Ho Yoon

_____

Seung-Jea Tahk

_____

Gyo-Seung Hwang

_____

So-Yeon Choi

_____

Se-Joong Rim

Ajou Graduate School, Ajou University

December, 22th, 2017

-ABSTRACT-

Prognostic Impact of Left Ventricular Mass Change
in Patients with ST-elevation Myocardial Infarction

Background: Prognostic significance between progression of left ventricular hypertrophy (LVH) and clinical outcomes in patients with ST-elevation myocardial infarction (STEMI) is uncertain. The objective of this study was to investigate prognostic impact of progression of LV mass index (LVMI) in patients with STEMI.

Methods: We analyzed the data and clinical outcomes of patients with STEMI who received successful coronary intervention. A total of 200 patients who had echocardiographic follow-up between 12 and 36 months were finally enrolled. According to change in LVMI compared to baseline LVMI, patients were classified into progression group and non-progression group. Progression of LVMI was defined when increment of LMVI was greater than 10% compared to baseline LVMI. End points were major adverse cardiac events within 5 years, including death, recurrent MI, target vessel revascularization, and hospitalization due to heart failure.

Results: Progression of LVMI occurred in 55 patients. In the progression group, rate of recurrent MI was higher (13 vs. 2 %, $P = 0.026$) and the event-free survival of recurrent MI was significantly worse (log-rank $P < 0.001$) than that in the non-progression group. Adjusted hazard ratio of progression of LVMI for recurrent MI was 10.253 (95% confidence intervals 2.019-52.061, $P = 0.005$).

Conclusion: Increased LVMI was an independent predictor for adverse events, especially for recurrent MI, in patients with STEMI.

Keyword: Left Ventricular Hypertrophy, Myocardial Infarction, Prognosis

List of Text

List of Figures

iii

List of Tables

I. INTRODUCTION

Left ventricular hypertrophy (LVH) is closely related to adverse cardiovascular events in various etiologies (Levy et al., 1990; Bombelli et al., 2009; Cuspidi et al., 2014). We have previously reported that LVH is associated with increased rate of adverse clinical outcomes in 30-day survivors after ST-elevation myocardial infarction (STEMI) with successful percutaneous coronary intervention (PCI) (Park et al., 2015). In the previous study, we examined the prognostic significance of LVH only at baseline without evaluating the impact of their serial changes. The progression or regression of LVH might affect the clinical outcomes. However, prognostic significance between progression of LVH and clinical outcomes in patients with STEMI has not been established yet. Therefore, the objective of this study was to determine the prognostic impact of progression of LVH in patients with STEMI.

II. Material and Method

A. Subject Population

We consecutively enrolled 30-day survivors after STEMI who underwent successful revascularization. Successful revascularization was defined as thrombolysis in myocardial infarction trial (TIMI) grade 3 flow and < 30% residual stenosis in infarct related artery after primary PCI. Transthoracic echocardiography was performed within 48 hours of primary PCI. We finally enrolled 200 patients (133 males, 56 ± 11 year-old) with echocardiographic follow-up (F/U) between 12 and 36 months after index STEMI. Medical records of all patients were retrospectively reviewed. This study was approved by the Ajou University Hospital Institutional Review Board (approval number: AJIRB-MED-MDB-17-015). We excluded patients from this study if they had history of prior revascularization. We also excluded patients if the LV dysfunction was caused by any of the following: predisposing cardiomyopathy, severe valvular heart disease including symptomatic aortic stenosis, or more than moderate aortic and mitral regurgitation.

B. Definition of Left Ventricular Mass and its Progression

Left ventricular mass (LVM) was calculated according to Devereux's formula
(Devereux et al., 1986) using linear measurements derived from two-dimensional echocardiography (Lang et al., 2005):

LVM (g) =0.8 x (1.04 x [(LV internal diastolic diameter + posterior wall thickness in diastole + septal wall thickness in diastole)^3-(LV internal diastolic diameter)^3] + 0.6

LVM was indexed to body surface area. According to the changes in LVMI compared

2

to baseline LVMI, patients were classified into progression group and non-progression group. Progression of LVMI was defined when increment of LMVI was greater than 10% compared to baseline LVMI.

C. Study End-points

End points of the present study were major adverse cardiac events (MACEs) within five years, including death, recurrent myocardial infarction (MI), target vessel revascularization (TVR), and hospitalization due to heart failure (HF). Recurrent myocardial infarction was defined according to the universal definition of MI (Thygesen et al., 2007). Target vessel revascularization was defined as clinically indicated percutaneous or surgical revascularization of the index vessel during follow-up. At five years after index STEMI, follow-up data were obtained by reviewing medical records and/or telephone interview with patients. To demonstrate a correlation between progression of LVH and long-term clinical outcomes, we enrolled the patients from 2003 to 2009, who were followed up for more than 5 years.

D. Statistical analysis

SPSS 13.0 statistical software package (SPSS Inc., Chicago, IL, USA) was used for all analyses. Data are shown as mean ± standard deviation for continuous variables or numbers and percentages for categorical variables. Comparisons were conducted by unpaired Student's t test for continuous variables or Pearson chi-square test for categorical variables. Event free survival analysis for patients in these groups was performed using the Kaplan-Meier method. Differences between groups were assessed by log-rank test. To assess adjusted relative hazard ratio (HR) of progression of LVMI to the study end points, Cox's proportional hazard model was used with potential variables associated with clinical outcomes. Adjusted covariates for the Cox's proportional hazard model were well-known predictors of MACEs such as age, gender,

3

diabetes mellitus, hypertension, smoking, dyslipidemia, Killip classification, LV ejection fraction (EF), and progression of LVMI. Results of Cox's regression analysis were expressed as adjusted HRs with 95% confidence intervals (CI) for clinical outcomes. Multivariate logistic regression analysis was performed to assess the effect of the presence of progression of LVMI on clinical outcomes. Null hypotheses of no difference were rejected if *P* values were less than 0.05.

III. Results

From 2003 to 2009, a total of 200 patients (164 males, 56 ±11 year-old) were enrolled. Mean value of baseline LVMI of these 200 patients was at 114 ± 30 g/m^2. Baseline LVMI showed normal distribution. Progression of LVMI occurred in 55 patients (41 males, 58 ± 12 year-old). Fifty-five patients (27.5%) were included in the progression group while the remaining 145 patients (72.5%) were included in the non-progression group.

Baseline clinical characteristics according to the two groups are summarized in Table 1. There were no statistical differences in baseline characteristics such as medical history or medical treatments between the two groups.

Patients with three-vessel disease were more common in the progression group ($P = 0.02$, Table 2) while patient with two-vessel disease were more common in the non-progression group ($P = 0.014$). Overall, patients with multi-vessel disease were not statistically different between the two groups. Distributions of culprit lesion and procedural type were also similar between the two groups.

Baseline LVMI was significantly lower in the progression group compared to that in the non-progression group (99 ± 23 vs. 120 ± 30 g/m^2, $P < 0.001$, Table 3). LV systolic function measured by EF and LV regional function measured by wall motion score index (WMSI) in the progression group were similar to those in the non-progression LVMI group (EF: 50 ± 9 vs. 50 ± 10 %, P = 0.775; WMSI: 1.53 ± 0.3 vs. 1.54 ± 0.35, P = 0.149). Parameters indicating LV chamber size such as LV end diastolic dimension (LVEDD) and LV end diastolic volume (LVEDV) were also similar between the two groups (49 ± 4 vs. 51 ± 5 mm, $P = 0.457$ and 94 ± 24 vs. 91 ± 25 mL, $P = 0.708$, respectively).

Table 1. Baseline characteristics.

	Non-progression group (n=145)	Progression group (n=55)	*P*
Age, years	55 ± 11	58 ±12	0.182
Male , No (%)	123 (85)	41 (75)	0.125
Body mass index, kg/m^2	24 ± 3	25 ± 3	0.602
Body surface area, g/m^2	1.8 ± 0.2	1.7 ± 0.2	0.124
Hypertension, No (%)	55 (38)	22 (40)	0.79
Diabetes, No (%)	33 (23)	6 (11)	0.118
Dyslipidemia, No (%)	15 (10)	9 (16)	0.289
Any smoking, No (%)	98 (68)	31 (56)	0.153
Previous CVA, No (%)	5 (3)	2 (4)	0.949
Medication			
RAS blocker, No (%)	142 (98)	51 (93)	0.167
β-blocker, No (%)	105 (72)	39 (71)	0.833
CCB, No (%)	16 (11)	5 (9)	0.691
Statin, No (%)	115 (79)	46 (84)	0.493
Laboratory data			
eGFR, ml/min/1.73m^2	9.4±4.4	10.7±4.9	0.143
LDL cholesterol, mg/dL	7.4±1.0	7.8±1.0	0.069
hs-CRP, mg/dL	6.4±2.1	5.7±2.0	0.114
Killip Class			
Killip clss 3, No (%)	6 (4)	5 (9)	0.248
Killip clss 4, No (%)	5 (3)	1 (2)	0.549

Values are mean ± standard deviation (SD)
CVA = cerebrovascular accident, RAS = renin-angiotensin system, CCB = calcium channel blocker,　eGFR = estimated glomerular filtration rate, LDL = low-density lipoprotein, hs-CRP = high sensitivity C-reactive protein

Table 2. Baseline angiographic characteristics.

	Non-progression group (n=145)	Progression group (n=55)	*P*
Culprit lesion			
LAD, No (%)	81 (56)	29 (53)	0.692
LCX, No (%)	10 (7)	4 (7)	0.926
RCA, No (%)	51 (35)	22 (40)	0.529
LM, No (%)	3 (2)	0 (0)	0.083
Coronary Artery Disease			
1 vessel disease, No (%)	61 (42)	24 (44)	0.842
2 vessel disease, No (%)	63 (43)	14 (26)	0.014
3 vessel disease, No (%)	21 (15)	17 (31)	0.02
Procedural type			
POBA, No (%)	1 (1)	1 (2)	0.476
BMS, No (%)	13 (9)	3 (6)	0.416
DES, No (%)	132 (91)	51 (93)	0.703

LAD = left anterior descending artery, LCX = left circumflex artery, RCA = right coronary artery, LM = left main artery, PCI = primary coronary intervention, POBA = plain old balloon angioplasty, BMS = bare metal stent, DES = drug eluting stent

Table 3. Baseline echocardiographic characteristics.

	Non-progression group (n=145)	Progression group (n=55)	*P*
LVEDD, mm	51 ± 5	49 ± 4	0.457
LVESD, mm	35 ± 7	34 ± 11	0.975
IVST, mm	11 ± 2	10 ± 2	0.045
PWT, mm	11 ± 2	10 ± 2	< 0.001
RWT	0.45 ± 0.09	0.4 ± 0.09	0.001
LVEDV, mL	91 ± 25	94 ± 24	0.577
LVESV, mL	46 ± 16	48 ± 16	0.688
LVEF, %	50 ± 10	50 ± 9	0.775
LV mass, g	210 ± 58	171 ± 42	< 0.001
LVMI, g/m^2	120 ± 30	99 ± 23	< 0.001
WMSI	1.54 ± 0.35	1.53 ± 0.3	0.149

Values are mean ± standard deviation (SD)
LVEDD = left ventricular end diastolic dimension, LVESD = left ventricular end systolic dimension, IVST = interventricular septal thickness at end diastole, PWT = posterior wall thickness at end diastole, RWT = relative wall thickness, LVEDV = left ventricular end diastolic volume, LVESV = left ventricular end systolic volume, LVEDVI = left ventricular end diastolic volume index, LVESVI = left ventricular end systolic volume index, LVEF = left ventricular ejection fraction, LVMI = left ventricular mass index, WMSI = wall motion score index

Mean changes of LVMI in the progression group and those in the non-progression group were $28 \pm 14\%$ and -12 ± 15 %, respectively. Follow-up echocardiography showed that LVMI was significantly higher in the progression group than that in the non-progression group (122 ± 25 vs. 104 ± 22 g/m^2, $P < 0.001$, Table 4). LV systolic and regional functions were maintained in both groups (EF: 53 ± 12 vs. 53 ± 11 %, $P = 0.966$; WMSI: 1.4 ± 0.35 vs. 1.39 ± 0.38, $P = 0.954$). In the progression group, LVEDD and LVEDV, parameters indication LV chamber size, showed progressive LV remodeling compared to those in the non-progression group (53 ± 5 vs. 51 ± 2 mm, $P = 0.046$; 131 ± 28 vs. 113 ± 36 mL, $P = 0.035$, respectively).
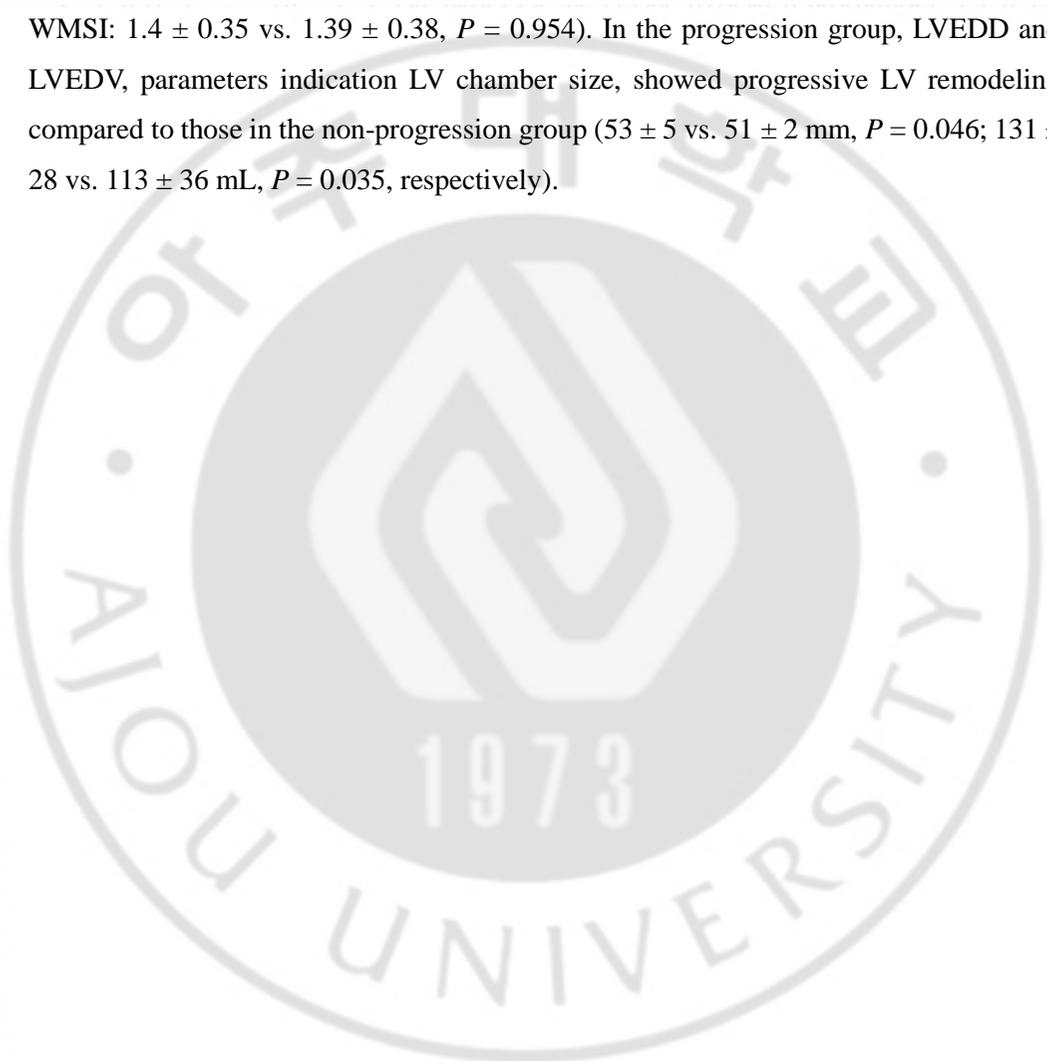
Table 4. Follow-up echocardiographic characteristics

	Non-progression group (n=145)	Progression group (n=55)	P
LVEDD, mm	51 ± 2	53 ± 5	0.046
LVESD, mm	36 ± 9	37 ± 8	0.176
IVST, mm	10 ± 2	10 ± 1	0.004
PWT, mm	10 ± 2	10 ± 1	0.022
RWT	0.38 ± 0.09	0.39 ± 0.07	0.372
LVEDV, mL	113 ± 36	131 ± 28	0.035
LVESV, mL	58 ± 27	70 ± 21	0.065
LVEF, %	53 ± 11	53 ± 12	0.966
LV mass, g	181 ± 42	210 ± 46	< 0.001
LVMI, g/m^2	104 ± 22	122 ± 25	< 0.001
WMSI	1.39 ± 0.38	1.4 ± 0.35	0.954

Values are mean ± standard deviation (SD)
LVEDD = left ventricular end diastolic dimension, LVESD = left ventricular end systolic dimension, IVST = interventricular septal thickness at end diastole, PWT = posterior wall thickness at end diastole, RWT = relative wall thickness, LVEDV = left ventricular end diastolic volume, LVESV = left ventricular end systolic volume, LVEDVI = left ventricular end diastolic volume index, LVESVI = left ventricular end systolic volume index, LVEF = left ventricular ejection fraction, LVMI = left ventricular mass index, WMSI = wall motion score index

Patients were followed up for 47 ± 16 months after index STEMI. MACEs occurred in 37 patients (19%). Of 200 patients, 15 (8%) died, 10 (5%) experienced recurrent MI, 19 (10%) needed TVR and 5 (3%) were hospitalized due to HF. Occurrences of MACEs, death, TVR and hospitalization due to HF were similar between the two groups (26 vs. 16 %, 7 vs. 8 %, 15 vs. 8 % and 6 vs. 1 % respectively). Rate of recurrent MI was higher in the progression group than in the non-progression group (13 vs. 2 %, $P = 0.026$). Event-free survival of recurrent MI was significantly worse in the progression group than in the non-progression group (log-rank $P < 0.001$, Figure 1).
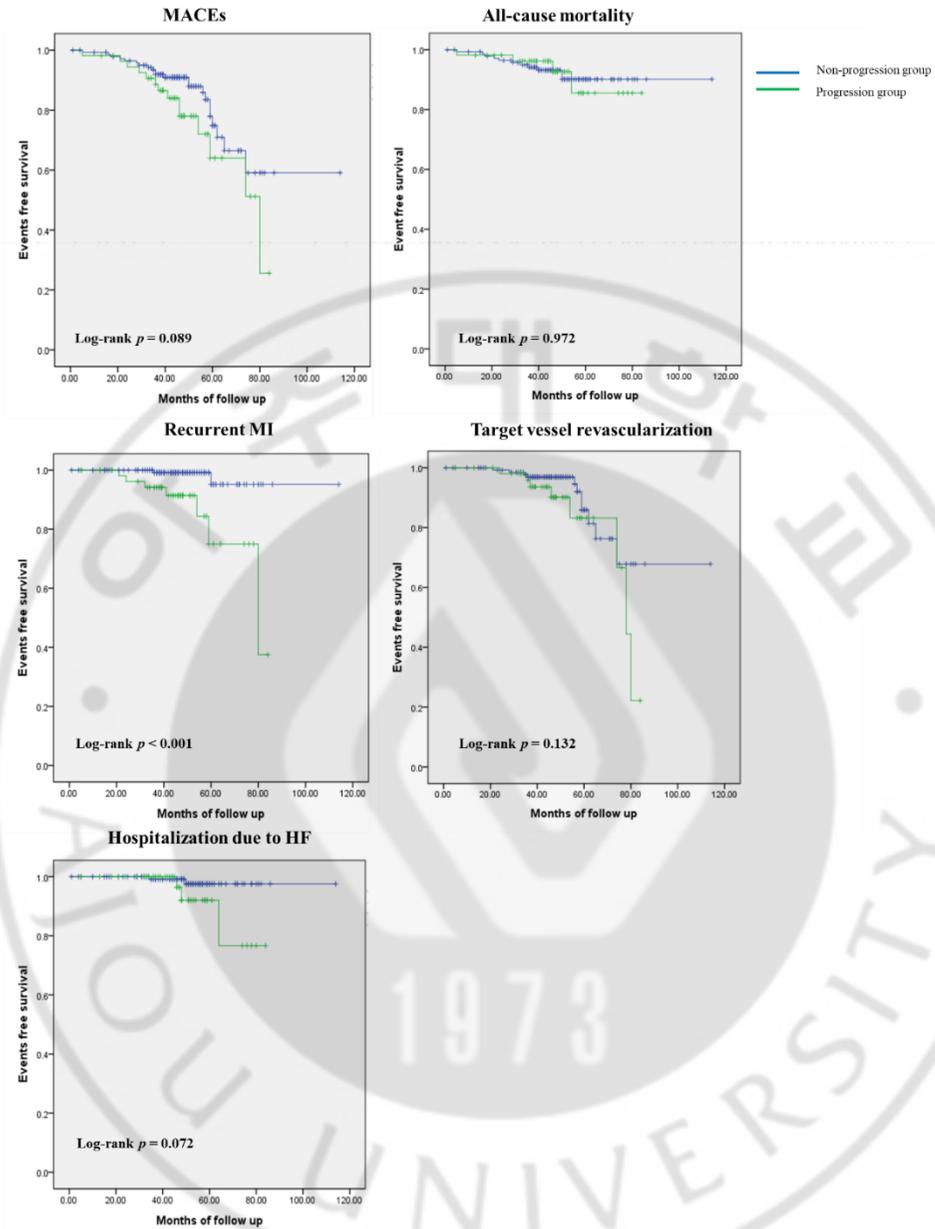
Fig 1. Kaplan-Meier survival curves for free of adverse outcomes in non-progression group and progression group.

MACEs = major adverse cardiovascular events, MI = myocardial infarction, HF = heart failure

Results of multivariate survival analysis using Cox's regression model are summarized in Table 5. In Cox's proportional hazard model, LVEF (HR 0.956, 95% CI 0.92-0.994, P = 0.023) and progression of LVMI (HR 2.466, 95% CI 1.175-5.174, P = 0.017) were related to MACEs. Age was strongly related to all cause of death (HR 1.1, 95% CI 1.03-1.175, P = 0.004). Adjusted HR of progression of LVMI for recurrent MI was 10.253 (95% CI 2.019-52.061, P = 0.005). LVEF (HR 0.926, 95% CI 0.869-0.987, P = 0.019) and progression of LVMI (HR 3.709, 95% CI 1.257-10.945, P = 0.018) were related to TVR. In a multivariate regression model, progression of LVMI was independently associated with increased risk for recurrent MI (HR 10.833, 95% CI 1.313-89.418, P = 0.027, Table 6).

Table 5. Cox's regression analysis for the adverse outcomes.

Variable	Adjusted Hazard ratio (95% CI)	*P*
MACEs		
Age	1.026 (0.99-1.062)	0.154
Gender	0.81 (0.276-2.377)	0.701
Hypertension	0.536 (0.247-1.16)	0.113
Diabetes	0.705 (0.301-1.647)	0.419
Dyslipidemia	3.670 (0.475-28.37)	0.213
Smoking	0.442 (0.179-1.09)	0.076
Killip classification	0.924 (0.594-1.438)	0.726
LVEF	0.956 (0.92-0.994)	0.023
Progression of LVMI	2.466 (1.175-5.174)	0.017
All-cause mortality		
Age	1.1 (1.030-1.175)	0.004
Gender	1.675 (0.341-8.238)	0.526
Hypertension	0.679 (0.214-2.15)	0.51
Diabetes	0.959 (0.243-3.785)	0.953
Dyslipidemia	352307.965 (0)	0.984
Smoking	0.505 (0.145-1.76)	0.284
Killip classification	0.958 (0.532-1.725)	0.885
LVEF	0.956 (0.902-1.014)	0.132
Progression of LVMI	1.029 (0.309-3.434)	0.963
Recurrent MI		
Age	1.005 (0.939-1.076)	0.875
Gender	2.354 (0.121-45.689)	0.571
Hypertension	0.549 (0.106-2.836)	0.474
Diabetes	57789.182 (0-6.364E194)	0.961
Dyslipidemia	1.135 (0.096-13.438)	0.92
Smoking	0.522 (0.072-3.809)	0.522
Killip classification	0.806 (0.273-2.376)	0.696
LVEF	0.996 (0.931-1.065)	0.902
Progression of LVMI	10.253 (2.019-52.061)	0.005
TVR		
Age	0.993 (0.948-1.041)	0.778
Gender	0.581 (0.114-2.965)	0.514
Hypertension	0.423 (0.128-1.391)	0.157
Diabetes	0.44 (0.135-1.432)	0.173
Dyslipidemia	5900004.378(0)	0.979
Smoking	0.392 (0.102-1.51)	0.173
Killip classification	0.786 (0.371-1.666)	0.529
LVEF	0.926 (0.869-0.987)	0.019
Progression of LVMI	3.709 (1.257-10.945)	0.018
Hospitalization due to HF		
Age	1.036 (0.903-1.189)	0.611
Gender	0.004 (0-4.162)	0.119
Hypertension	0.051 (0.001-3.203)	0.159
Diabetes	0.015 (0-1.64)	0.08
Dyslipidemia	8.326E7 (0)	0.982
Smoking	0.017 (0-8.227)	0.197
Killip classification	0.664 (0.125-3.538)	0.631

LVEF	0.74 (0.545-1.005)	0.054
Progression of LVMI	267.439 (0.843-84801.068)	0.057

MACEs = major adverse cardiovascular events, LVEF = left ventricular ejection fraction, LVMI = left ventricular mass index, MI = myocardial infarction, TVR = target vessel revascularization, HF = heart failure, CI = confidence interval

Table 6. Multivariate logistic regression analysis of the presence of progression of left ventricular mass index for clinical outcomes.

Variable	Hazard ratio (95% CI)	*P*
MACEs	0.459 (0.054-3.876)	0.474
All-cause mortality	1.285 (0.139-11.921)	0.825
Recurrent MI	10.833 (1.313-89.418)	0.027
TVR	2.869 (0.432-19.432)	0.275
Hospitalization due to HF	5.822 (0.859-39.478)	0.071

MACEs = major adverse cardiovascular events, MI = myocardial infarction, TVR = target vessel revascularization, HF = heart failure, CI = confidence interval

IV. Discussion

The present study demonstrated that change of LVMI was associated with clinical outcomes in patients with STEMI who received successful PCI. After index STEMI, LV remodeling is divided into an early phase (within 72 hours) and a late phase (beyond 72 hours). Early remodeling is induced by acute loss of myocardium, resulting in abrupt increase in loading conditions (Sutton et al., 2000). In our previous study, LVH at index STEMI is associated with increased rate of adverse clinical outcomes, especially all-cause mortality. Myocardial structural and functional alterations beyond EF representing LV systolic function might affect adverse clinical outcomes in patients with early remodeling (Park et al., 2015). Late remodeling, including LVH and alterations in ventricular architecture, is an adaptive response that can offset chronically increased hemodynamic load, attenuate progressive dilatation, and stabilize contractile function (Pfeffer et al., 1980). The progression of LVMI was related to increased risk for recurrent MI in the present study. In Cox's proportional hazard model, progression of LVMI was related to recurrent MI and TVR. Progression of LVMI might be more closely related to coronary vascular complication.

Myocyte hypertrophy is initiated by activation of neurohormonal system with local tissue renin-angiotensin (RAS) system and myocardial stretch. After MI, decreased cardiac output enhances cathecholamine production by adrenal medulla and sympathetic nerve terminals. It also activates RAS-aldosterone axis (Sutton et al., 2000). Stimulation of α1 adrenoreceptor by enhanced norepinephrine (NE) release, and angiotensin 1 receptor can induce myocyte hypertrophy via Gqα-dependent pathway which is upregulated in the viable border and scar tissue in post-MI hearts (Ju et al., 1998). Both NE and angiotensin II augment endothelin-1 release, which is another stimulus for myocyte hypertrophy (Levin et al., 1998). Mechanical myocardial stretch induced by elevated wall stresses sensed by infarcted and non-infarcted myocardium can result in secretion of angiotensin II from cytoplasmic granules and induce myocyte hypertrophy

mediated by angiotensin 1 receptor (Yamazaki et al., 1995).

In atherosclerotic plaque lesions, local RAS system is also activated. Angiotensin II can induce myocyte hypertrophy. It can also generates oxidative stress in vessel wall, resulting in stimulation of vascular thrombosis and inflammation (Mehta et al., 2007). In vascular smooth muscle cells, exposure to angiotensin II leads to increased levels of plasminogen-activator inhibitor type 1 which can inhibit tissue plasminogen activator and urokinase, and cell adhesion molecules such as vascular cell adhesion molecule-1 and intercellular adhesion molecule-1, resulting in prothrombotic status (Feener et al., 1995). In angiotensin II stimulated vascular smooth muscle cells, effects of inflammatory cytokine interleukin-18 are enhanced. This is related to progression of atherosclerosis and restenosis (Gerdes et al., 2002).

Pathologic angiotensin II-induced signaling in vascular, endothelial and cardiac cells can promote vascular thrombosis, neointima formation and LVH. In the present study, close correlation between progression of LVMI and adverse clinical outcomes, especially recurrent MI, might be affected by pathologic angiotensin-II signaling. Many studies have demonstrated that RAS blocker can prevent angiotensin II-induced LVH and vascular pathology (Kim et al., 1995; Keidar et al., 1997; 18. Yusuf et al., 2000), Therefore, RAS blocker might be able to reduce adverse long-term clinical outcomes in patients with progression of LVMI after index STEMI.

This study has several limitations. First, echocardiographic measuring LVM using linear measurements has potential limitations. It is based on the assumption that the LV is represented by a prolate ellipse (Devereux et al., 1986). Nevertheless, LVM obtained with this method has been well validated and widely used in clinical practice (Lang et al., 2005). Although there could be geometrical deformation, we measured LVMI at index STEMI and follow-up using same technical method and analyzed the presence of change in LVMI not the value of LMVI itself. Second, there is no validated definition of

progression of LVMI. In the present study, we defined progression of LVMI as an increment of LMVI greater than 10% compared with baseline LVMI. There have been no data demonstrating association between progression of LVMI and clinical outcomes. Further study is needed to define clinically significant progression of LVMI. Third, the present study could not demonstrate a possible benefit of regression of LVMI. A total of 82 patients had LVMI regression in the present study. There was no significant correlation between regression of LVMI and MACEs. It might be due to the relatively small number of our study population. Fourth, levels of angiotensin II and related cytokines were not checked in the present study. The present study logically implied that angiotensin II had a pathological role in the progression group. To prove this, further studies might be needed to evaluate levels of angiotensin II and related cytokines. Finally, we could not fully evaluate the impact of serial changes of LVMI. Since the present study was retrospective and annual echocardiographic follow-up was not recommended after index STEMI in current guidelines, we enrolled patients with echocardiographic follow-up (F/U) between 12 and 36 months after index STEMI. We could not know the effect of rate of progression in LVMI.

V. Conclusion

In summary, increased LVMI was found to be an independent predictor for adverse events, especially for recurrent MI in patients with STEMI who received successful coronary intervention. Therefore, maintenance and dose-adjustment of proper medical treatment including RAS blocker should be considered in patients with progression of LVMI after index STEMI.

REFERENCES

1. Bombelli M, Facchetti R, Carugo S, Madotto F, Arenare F, Quarti-Trevano F, Capra A, Giannattasio C, Dell'Oro R, Grassi G, Sega R, Mancia G: Left ventricular hypertrophy increases cardiovascular risk independently of in-office and out-of-office blood pressure values. *J Hypertens* 27(12): 2458-2464, 2009.

2. Cuspidi C, Facchetti R, Bombelli M, Sala C, Grassi G, Mancia G: Differential Value of Left Ventricular Mass Index and Wall Thickness in Predicting Cardiovascular Prognosis: Data From the PAMELA Population. *Am J Hypertens* 27(8): 1079-1086, 2014.

3. Devereux RB, Alonso DR, Lutas EM, Gottlieb GJ, Campo E, Sachs I, Reichek N: Echocardiographic assessment of left ventricular hypertrophy: comparison to necropsy findings. *Am J Cardiol* 57(6): 450-458, 1986.

4. Feener EP, Northrup JM, Aiello LP, King GL: Angiotensin II induces plasminogen activator inhibitor-1 and -2 expression in vascular endothelial and smooth muscle cells. *J Clin Invest* 95(3): 1353-1362, 1995.

5. Gerdes N, Sukhova GK, Libby P, Reynolds RS, Young JL, Schönbeck U: Expression of interleukin (IL)-18 and functional IL-18 receptor on human vascular endothelial cells, smooth muscle cells, and macrophages: implications for atherogenesis. *J Exp Med* 195(2): 245-257, 2002.

6. Ju H, Zhao S, Tappia PS, Panagia V, Dixon IM: Expression of Gq alpha and PLC-beta in scar and border tissue in heart failure due to myocardial infarction. *Circulation* 97(9): 892-899, 1998.

7. Keidar S, Attias J, Smith J, Breslow JL, Hayek T: The angiotensin-II receptor antagonist, losartan, inhibits LDL lipid peroxidation and atherosclerosis in apolipoprotein E-deficient mice. *Biochem Biophys Res Commun* 236(3): 622-625, 1997.

8. Kim S, Ohta K, Hamaguchi A, Yukimura T, Miura K, Iwao H: Angiotensin II induces cardiac phenotypic modulation and remodeling in vivo in rats. *Hypertension* 25(6): 1252-1259, 1995.

9. Lang RM, Bierig M, Devereux RB, Flachskampf FA, Foster E, Pellikka PA, Picard MH, Roman MJ, Seward J, Shanewise JS, Solomon SD, Spencer KT, Sutton MS, Stewart WJ; Chamber Quantification Writing Group; American Society of Echocardiography's Guidelines and Standards Committee; European Association of Echocardiography: Recommendations for chamber quantification: a report from the American Society of Echocardiography's Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. *J Am Soc Echocardiogr* 18(12): 1440-1463, 2005.

10. Levin ER, Gardner DG, Samson WK: Natriuretic peptides. *N Engl J Med* 339(5): 321-328, 1998.

11. Levy D, Garrison RJ, Savage DD, Kannel WB, Castelli WP: Prognostic implications of echocardiographically determined left ventricular mass in the Framingham Heart Study. *N Engl J Med* 322(22): 1561-1566, 1990.

12. Mehta PK, Griendling KK: Angiotensin II cell signaling: physiological and pathological effects in the cardiovascular system. *Am J Physiol Cell Physiol* 292(1): C82-C97, 2007.

13. Park JS, Shin JS, Lee YH, Seo KW, Choi BJ, Choi SY, Yoon MH, Hwang GS, Tahk SJ, Shin JH: Left ventricular hypertrophy on long-term cardiovascular outcomes in patients with ST-elevation myocardial infarction. *Clin Exp Hypertens* 37(8): 674-679, 2015.

14. Pfeffer MA, Braunwald E: Ventricular remodeling after myocardial infarction. Experimental observations and clinical implications. *Circulation* 81(4): 1161-1172, 1990.

15. Sutton MG, Sharpe N: Left ventricular remodeling after myocardial infarction:

pathophysiology and therapy. *Circulation* 101(25): 2981-2988, 2000.

16.   Thygesen K, Alpert JS, White HD; Joint ESC/ACCF/AHA/WHF Task Force for the Redefinition of Myocardial Infarction, Jaffe AS, Apple FS, Galvani M, Katus HA, Newby LK, Ravkilde J, Chaitman B, Clemmensen PM, Dellborg M, Hod H, Porela P, Underwood R, Bax JJ, Beller GA, Bonow R, Van der Wall EE, Bassand JP, Wijns W, Ferguson TB, Steg PG, Uretsky BF, Williams DO, Armstrong PW, Antman EM, Fox KA, Hamm CW, Ohman EM, Simoons ML, Poole-Wilson PA, Gurfinkel EP, Lopez-Sendon JL, Pais P, Mendis S, Zhu JR, Wallentin LC, Fernández-Avilés F, Fox KM, Parkhomenko AN, Priori SG, Tendera M, Voipio-Pulkki LM, Vahanian A, Camm AJ, De Caterina R, Dean V, Dickstein K, Filippatos G, Funck-Brentano C, Hellemans I, Kristensen SD, McGregor K, Sechtem U, Silber S, Tendera M, Widimsky P, Zamorano JL, Morais J, Brener S, Harrington R, Morrow D, Lim M, Martinez-Rios MA, Steinhubl S, Levine GN, Gibler WB, Goff D, Tubaro M, Dudek D, Al-Attar N: Universal definition of myocardial infarction. *Circulation* 116 (22): 2634-2653, 2007.

17.   Yamazaki T, Komuro I, Kudoh S, Zou Y, Shiojima I, Mizuno T, Takano H, Hiroi Y, Ueki K, Tobe K, Kadowaki T, Nagai R, Yazaki Y: Angiotensin II partly mediates mechanical stress-induced cardiac hypertrophy. *Circ Res* 77(2): 258-265, 1995.

18.   Yusuf S, Sleight P, Pogue J, Bosch J, Davies R, Dagenais G: Effects of an angiotensin-converting-enzyme inhibitor, ramipril, on cardiovascular events in high-risk patients. *N Engl J Med* 342(3): 145-153, 2000.

ST 분절 상승 심근경색증 환자에서
좌심실 질량 변화의 임상적 의의

목적: ST 분절 상승 심근경색증 환자에서 좌심실 질량 변화와 주요심장사건 발생에 대한 연구는 이루어지지 않았다. 본 연구는 ST 분절 상승 심근경색증 환자에서 좌심실 질량 지수의 변화가 예후에 영향을 미치는 지에 대해 조사하였다.

방법: 성공적인 일차적 관동맥 중재시술을 받은 ST 분절 상승 심근경색증 환자의 임상 데이터를 분석하였다. ST 분절 상승 심근경색증 진단 후 12개월에서 36개월 사이에 심초음파 추적관찰을 시행한 총 200명의 환자를 최종적으로 연구에 등록하였다. 심초음파 추적 검사에서 좌심실 질량지수의 증가 여부에 따라 환자의 군을 분류하였다. 좌심실 질량지수의 증가는 입원 당시 측정한 좌심실 질량지수와 비교하여 10% 이상의 좌심실 질량지수 증가가 있을 때로 정의하였다. 5년 이내의 환자의 사망, 재발성 심근경색, 표적 혈관의 재 개통, 심부전에 의한 입원으로 구성된 주요 심장사건을 연구하였다.

결과: 55명의 환자에서 좌심실 질량지수의 증가가 있었다. 좌심실 질량지수의 증가가 있었던 환자군에서, 재발성 심근경색의 발생율이 좌심실 질량지수의 증가가 없었던 환자군보다 높았고 (13 vs. 2 %, $P = 0.026$) 재발성 심근경색 무사건 생존률은 통계적으로 의미있게 낮았다(log−rank $P < 0.001$). 좌심실 질량지수의 증가와 재발성 심근경색에 대한 비교 위험도는 10.253 (95% 신뢰구간 2.019−52.061, $P = 0.005$) 이었다.

결론: ST 분절 상승 심근경색증 환자에서 좌심실 질량 지수의 증가는 주요
심장 사건 중 특히 재발성 심근경색과 연관성이 있었다.