Prediction of Infarct Transmurality From C-Reactive Protein Level and Mean Platelet Volume in Patients With ST-Elevation Myocardial Infarction: Comparison of the Predictive Values of Cardiac Enzymes

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Background: High C-reactive protein (CRP) and mean platelet volume (MPV) levels are associated with poor prognosis in patients with ST-segment elevation myocardial infarction (STEMI). The aim of this study was to evaluate the relationship between CRP level or MPV and infarct transmural involvement in patients with STEMI. **Methods:** We retrospectively reviewed CRP level, MPV, and infarct transmural involvement in 112 STEMI patients who were assessed with contrast-enhanced cardiac magnetic resonance imaging. **Results:** When the cut-off peak CRP level and MPV were set at 2.35 mg/dl and 7.3 fl using receiver operating characteristic curves analysis, the sensitivity was 67.3/69.2% and specificity was 76.7/76.7% for differentiating between the groups with and those without transmural involvement. Peak CRP level, MPV, peak creatine kinase-MB (CK-MB) level, and peak high-sensitivity cardiac

troponin T (hs-cTnT) level had comparable predictive values for transmural involvement (area under the curve, 0.749, 0.761, 0.680, and 0.696, respectively). High peak CRP level and MPV were independent predictors of transmural involvement after adjusting for the peak CK-MB level, peak hs-cTnT level, baseline thrombolysis in myocardial infarction flow grade, and left ventricular ejection fraction (odds ratio: 5.16/5.42, 95% confidence interval: 1.84–14.50/2.03–14.47, $P = 0.002/0.001$, respectively) in the logistic regression analysis. **Conclusion:** The results of this study show that peak CRP level and MPV are predictive markers for transmural involvement. Their predictive power for transmural involvement is independent of and comparable to that of peak CK-MB and hs-cTnT levels. J. Clin. Lab. Anal. 30:930–940, 2016. © 2016 Wiley Periodicals, Inc.

Key words: C-reactive protein; mean platelet volume; myocardial infarction; magnetic resonance imaging

INTRODUCTION

Mean platelet volume (MPV), the most commonly used measure of platelet size, is an indicator of platelet reactivity (1–5). Recently, a meta-analysis reported that higher MPV is related to coronary artery disease (6). Moreover, MPV is a predictor of cardiovascular risk, quantified on automated hemograms, and is routinely measured prior to coronary revascularization (2, 5, 7, 8). High preprocedural MPV is associated with increased mortality in patients with ST-segment elevation myocardial infarction (STEMI) (9).

In acute myocardial infarction (AMI), ischemia-reperfusion damage and mechanical stress cause acute

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inflammation (10). Excessive systemic inflammatory activity may hamper tissue repair, enhance apoptosis at the margin of the infarcted tissue, and increase the risk of short- or long-term mortality (11–14). C-reactive protein (CRP), a systemic indicator of inflammation, is the established acute-phase protein that attaches to ligands exposed in injured tissue and stimulates the complement system (15–17). During AMI, circulating CRP levels rise after the onset of ischemia (18–20). Peak CRP concentration measured 24–72 hr following symptom onset is considered a significant prognostic indicator of 1-year outcomes (21, 22).

Contrast-enhanced cardiac magnetic resonance (CE-CMR) imaging is gaining approval and being increasingly used for application in quantifying the at-risk or chronically injured myocardium following STEMI, and can identify and display infarct size and transmural-ity, myocardial area at risk (AAR), myocardial viability, microvascular obstruction, and myocardial hemorrhage (23–29). CE-CMR imaging parameters appear to be related to abnormal electrocardiograms in anterior AMI patients (30).

The predictive values of CRP and MPV for infarct transmural-ity using CE-CMR imaging in patients with STEMI have not been studied. The aim of this study was to determine the relationship between peak CRP level/MPV and infarct transmural-ity using CE-CMR imaging in STEMI patients.

MATERIALS AND METHODS

Subjects

A total of 374 consecutive patients with STEMI who underwent measurement of CRP level and MPV between November 2010 and July 2014 were enrolled in this study. Patients were included if they were older than 18 years and had undergone primary percutaneous coronary intervention (PCI) within 12 hr after symptom onset. Patients who did not give consent to undergo CE-CMR imaging or who had contraindications for CE-CMR imaging were excluded; 112 patients were finally included. The present study protocol was approved by the Chosun University Hospital Research Ethics Committee (approval CHOSUN 2014-12-001).

Definition of STEMI

STEMI was defined as an ST-segment elevation of at least 1 mm in two or more standard leads, at least 2 mm in two or more neighboring precordial leads, or presumed new-onset left bundle branch block.

Percutaneous Coronary Intervention

All patients received dual oral antiplatelet treatment (300 mg aspirin, 600 mg clopidogrel) prior to intervention, and maintenance doses of aspirin (100–200 mg daily) and clopidogrel (75 mg daily) thereafter. Coronary angiography and stent implantation were performed by standard interventional techniques. Glycoprotein IIb/IIIa receptor antagonists were administered intravenously as required.

Blood Collection and High-Sensitivity CRP (hsCRP) Level and MPV Measurement

Venous blood samples were collected in K₂-ethylenediaminetetraacetic acid (EDTA) and serum separator blood-drawing tubes (Becton Dickinson, Franklin Lakes, NJ) before and 24–72 hr after PCI, and on the day of discharge. hsCRP levels and MPV were analyzed within 2 hr after sample collection using a BN II System (Siemens Healthcare Diagnostics GmbH, Eschborn, Germany) and an ADVIA 2120 Hematology System (Siemens Healthcare Diagnostics GmbH), respectively.

CE-CMR Imaging Protocol and Analysis

A specified depiction of the CE-CMR procedure and techniques used for imaging has been stated elsewhere (31) and is outlined below. A complete CE-CMR study was carried out to assess myocardial infarction and cardiac function. Examinations were performed with a 1.5-T MR scanner (Avanto, Siemens Medical Solutions, Erlangen, Germany) and a 3.0-T MR scanner (Magnetom Skyra, Siemens Medical Solutions, Erlangen, Germany) with dedicated cardiac surface coils.

T2- and T1-weighted images were obtained as a stack of contiguous 8-mm thick images in the cardiac short-axis view. Cine images were acquired by a fast gradient echo sequence (steady state free precession) in the short-axis, 2-chamber, and 4-chamber views. The slice thickness was set at 8 mm without gaps, and short-axis images of the left ventricle (LV) were obtained from the apex to the base to contain the whole LV volume. Stress perfusion imaging was performed following scouting and cine imaging. Adenosine ($140 \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$) was infused for 6 min. Subsequently, a dosage of 0.2 mmol/kg gadolinium-diethylene triamine pentaacetic acid (Magnevist, Bayer Schering Pharma, Berlin, Germany) was infused intravenously at a speed of 3 ml/s followed by a 20 ml saline flush for 4 min under adenosine infusion. Delayed hyperenhancement and the extent of microvascular obstruction (MVO) were evaluated 5 and 15 min after contrast administration in 10–12 contiguous 8-mm thick slices with no gap. The field of view and image matrix were

224 × 340 mm (230 × 350 mm in 3T MR) and 256 × 146 (256 × 156 in 3T MR), respectively.

The entire cardiac MR image parameters were determined at our MRI core laboratory. LV end-diastolic volume (LVEDV), LV end-systolic volume (LVESV), and ejection fraction (EF) were calculated. Myocardial mass was analyzed by multiplying the myocardial volume by the myocardial density (1.05 g/ml). LV mass was indexed to the body surface area. Infarct volume of the LV was measured based on delayed enhancement. The volume and the extent of MVO, defined as a late hypoenhanced region within the infarcted myocardium on the delayed enhancement image, were calculated in the same manner as the infarct volume. The myocardial AAR was defined as myocardium with a signal intensity larger than 2 standard deviations (SDs) above the mean signal intensity of a distant normal myocardium and expressed as a percentage of LV myocardial volume. Myocardial salvage index was calculated as follows: myocardial salvage index = (AAR – infarct size) × 100/AAR. We analyzed infarct transmural extent for all segments by dividing the maximal hyperenhanced thickness by the full myocardial thickness in each segment. The transmural extent of infarction was expressed as >75% of infarct transmural extent.

Statistical Analysis

All values are expressed as means ± SDs/medians (interquartile ranges [IQRs]) or numbers (percentages). The Mann–Whitney *U*-test for continuous variables and chi-square (statistic) analysis for noncontinuous variables were used to compare baseline characteristics between groups.

Receiver operating characteristic (ROC) curve analysis was performed to determine the sensitivity and specificity with 95% confidence intervals (CIs) of the cutoff hsCRP level and MPV detecting the transmural extent of infarction. In addition, multivariable logistic regression analysis of factors associated with the transmural extent of infarction was performed using a forward conditional stepwise model. Baseline clinical factors with *P* values < 0.1 on univariate analysis were entered into the model. Independent variables included hsCRP ≥ 2.35 mg/dl, MPV ≥ 7.3 fl, peak CK-MB level, peak high-sensitivity cardiac troponin T (hs-cTnT) level, LVEF, and baseline thrombolysis in myocardial infarction (TIMI) flow grade. Relationships between hsCRP level or MPV and other clinical variables were evaluated using Pearson's correlation analysis. *P* values < 0.05 were considered statistically significant. All statistical analyses were performed using SPSS, version 15 for Windows (SPSS, Inc., Chicago, IL) and MedCalc 14.10.2 (MedCalc Software bvba, Acaciaaan, Ostend, Belgium).

RESULTS

Baseline Characteristics of the Cohort

Mean patient age was 59.0 years, and 85.7% patients were men. Other clinical, angiographic, and CE-CMR imaging characteristics of the overall cohort are shown in Table 1. Mean baseline and peak hsCRP levels for the overall study population were 1.60 ± 2.25 and 3.32 ± 4.43 mg/dl (median, 0.54 and 1.35 mg/dl; IQR, 0.20–2.20 and 0.30–5.07 mg/dl; normal range, 0.0–0.1 mg/dl), respectively. Mean MPV for the overall study population was 7.58 ± 1.16 fl (median, 7.30 fl; IQR, 6.80–8.00; normal range, 7.20–11.1 fl).

Cut-Off hsCRP Level and MPV for Predicting Transmural Extent of Infarction

Z-statistics for comparisons of individual ROC curves between baseline hsCRP and peak hsCRP levels were significantly different (Fig. 1A). The ROC curve analysis indicated a cut-off value of 2.35 mg/dl for peak hsCRP level, with 67.3% sensitivity (95% CI: 52.9–79.7) and 76.7% specificity (95% CI: 64.0–86.6; area under the ROC curve [AUC] = 0.749, *P* < 0.001), for the detection of transmural extent of infarction (Fig. 1B). ROC analysis indicated a cut-off value of 7.3 fl for MPV with 69.2% sensitivity (95% CI: 54.9–81.3) and 76.7% specificity (95% CI: 64.0–86.6; AUC = 0.761, *P* < 0.001) for the detection of transmural extent of infarction (Fig. 1B).

The mean peak hsCRP and MPV value was higher in patients with transmural extent of infarction (1.86 ± 2.98 vs. 5.01 ± 5.19 mg/dl, *P* < 0.001; 7.22 ± 1.07 vs. 7.99 ± 1.14, *P* < 0.001; Fig. 2) than in those without.

Clinical, Angiographic, and CE-CMR Imaging Data Based on Cut-Off Peak hsCRP Level

Patients were stratified into two groups according to the cut-off peak hsCRP values: peak hsCRP < 2.35 mg/dl (62 patients) and peak hsCRP ≥ 2.35 mg/dl (50 patients). The clinical, angiographic, and CE-CMR imaging data of these two groups are shown in Table 1. Although we noted that the proportion of men was higher in the high hsCRP level group than in the low hsCRP level group, these trends were not statistically significant. Initial heart rate and peak CK-MB and hs-cTnT levels in patients with high hsCRP levels were higher than those in patients with low hsCRP levels. Otherwise, there were no differences in clinical and demographic characteristics between the two groups. Patients with a high peak hsCRP level tended to develop angiographic no-reflow phenomenon and use glycoprotein IIb/IIIa inhibitors. A high rate of baseline TIMI flow grade 0–1 and low rate of final TIMI flow

TABLE 1. Baseline Characteristics, Angiographic Data, and CE-CMR Imaging Data on the Basis of Peak hsCRP Level

Characteristic	Total (n = 112)	Peak hsCRP <2.35 mg/dl (n = 62)	Peak hsCRP ≥2.35 mg/dl (n = 50)	P-value
Clinical characteristics				
Age (years)	59.0 ± 10.4	59.4 ± 10.5	58.6 ± 10.3	0.697
Male sex (%)	85.7	80.6	92.0	0.088
Hypertension (%)	41.1	46.8	34.0	0.172
Diabetes mellitus (%)	17.9	16.1	20.0	0.595
Dyslipidemia (%)	11.6	12.9	10.0	0.633
Smoking (%)	72.3	67.7	78.0	0.228
Prior PCI (%)	5.4	4.8	6.0	0.786
Killip class ≥2 (%)	51.8	45.2	60.0	0.118
Anterior infarction (%)	42.9	40.3	46.0	0.546
SBP at admission (mmHg)	126.1 ± 24.3	127.6 ± 23.2	124.2 ± 25.7	0.455
Initial heart rate (beat/min)	73.5 ± 17.1	70.6 ± 15.6	77.2 ± 16.2	0.042
Door to balloon time (min)	79.5 ± 21.3	82.1 ± 24.5	76.1 ± 16.2	0.150
Symptom to balloon time (min)	264.9 ± 166.7	261.5 ± 162.3	269.1 ± 173.7	0.811
Peak CK-MB (ng/dl)	222.1 ± 123.5	190.5 ± 115.7	261.3 ± 122.6	0.002
Peak hs-cTnT (ng/ml)	6.39 ± 3.78	5.08 ± 3.41	8.02 ± 3.60	<0.001
Creatinine (mg/dl)	1.00 ± 0.19	1.00 ± 0.18	1.00 ± 0.20	0.907
MPV (fl)	7.58 ± 1.16	7.42 ± 1.00	7.78 ± 1.32	0.102
Baseline hsCRP (mg/dl)	1.60 ± 2.25	0.48 ± 0.51	3.00 ± 2.76	<0.001
Peak hsCRP (mg/dl)	3.32 ± 4.43	0.54 ± 0.52	6.78 ± 4.69	<0.001
Angiographic data				
Culprit artery				
LAD (%)	42.9	40.3	46.0	0.546
LCx (%)	14.3	14.5	14.0	0.938
RCA (%)	42.9	45.2	40.0	0.583
Multivessel disease (%)	56.3	59.7	52.0	0.416
Baseline TIMI flow grade 0–1 (%)	79.5	69.4	92.0	0.003
Final TIMI flow grade 3 (%)	92.0	96.8	86.0	0.037
Angiographic no-reflow (%)	2.7	0.0	6.0	0.051
Thrombus aspiration (%)	23.2	21.0	26.0	0.531
Bare-metal stents (%)	24.1	21.0	28.0	0.387
Stent diameter at culprit artery, mm	3.13 ± 0.59	3.11 ± 0.57	3.15 ± 0.63	0.781
Stent length at culprit artery, mm	31.5 ± 18.0	30.6 ± 18.8	32.5 ± 17.2	0.599
Glycoprotein IIb/IIIa inhibitor (%)	57.1	50.0	66.0	0.089
CE-CMR imaging data				
LVEDV (ml)	140.1 ± 32.9	132.8 ± 31.1	149.1 ± 33.1	0.009
LVESV (ml)	70.4 ± 28.8	63.0 ± 24.9	79.7 ± 30.9	0.002
LV mass index (g/m ²)	89.1 ± 16.2	85.9 ± 14.0	93.5 ± 17.8	0.012
LV EF (%)	49.8 ± 9.8	52.9 ± 9.5	46.0 ± 8.9	<0.001
Infarct size, % of LV	6.88 ± 5.5	5.30 ± 4.5	8.83 ± 5.9	0.001
AAR, % of LV	17.4 ± 11.1	16.2 ± 11.3	18.9 ± 10.9	0.201
Myocardial salvage index (%)	0.58 ± 0.26	0.63 ± 0.27	0.53 ± 0.24	0.048
Hemorrhagic infarction (%)	0.57 ± 1.27	0.44 ± 0.93	0.74 ± 1.59	0.220
MVO area, % of LV	0.24 ± 0.55	0.16 ± 0.45	0.34 ± 0.64	0.096
Number of segments with >75% of infarct transmural	1.45 ± 1.73	0.94 ± 1.41	2.10 ± 1.88	<0.001
Maximal infarct transmural (%)	66.0 ± 29.0	55.8 ± 27.9	78.6 ± 25.3	<0.001
Frequency of transmural extent of infarction (%)	46.4	27.4	70.0	<0.001

^a“Smoking” means active smokers as well as ex-smokers who stopped smoking less than 1 year before enrollment.

hsCRP, high-sensitivity CRP; PCI, percutaneous coronary intervention; SBP, systolic blood pressure; CK, creatine kinase; hs-cTnT, high-sensitivity cardiac troponin T; MPV, mean platelet volume; LAD, left anterior descending coronary artery; LCX, left circumflex coronary artery; RCA, right coronary artery; TIMI, thrombolysis in myocardial infarction; CE-CMR, contrast-enhanced cardiac magnetic resonance; LV, left ventricle; LVEDV, left ventricular end-diastolic volume; LVESV, left ventricular end-systolic volume; MVO, microvascular obstruction.

Fig. 1. Receiver operating characteristics curves of baseline and peak high-sensitivity C-reactive protein (CRP) levels and mean platelet volume (MPV) for predicting transmural infarction. Comparison between baseline CRP and peak CRP levels (A); peak CRP level and MPV, respectively (B).

grade 3 were associated with high peak hsCRP level. There were no differences in other angiographic or procedural characteristics between the two groups.

CE-CMR imaging was performed at a median of 41 days after the index event (IQR, 31–52 days). No significant differences were found in the interval from procedure to CE-CMR imaging between the high peak hsCRP level group (47.6 ± 37.9 days) and the low peak hsCRP level

group (53.6 ± 57.2 days, $P = 0.529$). Figure 3 demonstrates representative coronary angiography before reperfusion and CE-CMR images of reperfused STEMI. CE-CMR imaging findings are presented in Table 1. LVEDV, LVESV, LV mass index, infarct size, number of segments with >75% of infarct transmural, and maximal infarct transmural were higher in the high peak hsCRP level group than in the low peak hsCRP level group on

Fig. 2. Peak high-sensitivity CRP level and mean protein volume according to transmural infarction categories.

CE-CMR imaging. In addition, LVEF and myocardial salvage index were lower and transmural extent of infarction was detected more frequently in the high peak hsCRP level group than in the low peak hsCRP level group. There was a trend of increased MVO area in the high peak hsCRP level group compared with that in the low peak hsCRP level group.

Clinical, Angiographic, and CE-CMR Imaging Data Based on Cut-Off MPV

Patients were stratified into two groups according to the cut-off MPV value: MPV < 7.3 fl (56 patients) and MPV ≥ 7.3 fl (56 patients). The clinical and demographic characteristics of these two groups are shown in Table 2. Although we noted that the prevalence of history of PCI

Fig. 3. An ST-elevation myocardial infarction patient with a culprit lesion in the right coronary artery. Coronary angiogram showing total occlusion of the proximal right coronary artery (A). T2-weighted short-axis image showing edema in the inferior wall and inferoseptum of the left ventricle (B) and corresponding delayed enhancement (C). Myocardial mass and other functional parameters derived from stacked images measured by endocardial and epicardial contours at diastole (right image in D) and systole (left image in D).

TABLE 2. Baseline Characteristics, Angiographic Data, and CE-CMR Imaging Data on the Basis of MPV

Characteristic	Total (n = 112)	MPV < 7.3 fl (n = 56)	MPV ≥ 7.3 fl (n = 56)	P-value
Clinical characteristics				
Age (years)	59.0 ± 10.4	59.7 ± 10.6	58.3 ± 10.2	0.498
Male gender (%)	85.7	82.1	89.3	0.280
Hypertension (%)	41.1	41.1	41.1	1.000
Diabetes mellitus (%)	17.9	16.1	19.6	0.622
Dyslipidemia (%)	11.6	12.5	10.7	0.768
Smoking (%)	72.3	67.9	76.8	0.291
Prior PCI (%)	5.4	1.8	8.9	0.093
Killip class ≥2 (%)	51.8	53.6	50.0	0.705
Anterior infarction (%)	42.9	46.4	39.3	0.445
SBP at admission (mmHg)	126.1 ± 24.3	128.6 ± 20.7	123.5 ± 27.4	0.266
Initial heart rate (beat/min)	73.5 ± 17.1	72.3 ± 16.5	74.8 ± 17.6	0.451
Door to balloon time (min)	79.5 ± 21.3	83.4 ± 26.3	75.6 ± 13.9	0.051
Symptom to balloon time (min)	264.9 ± 166.7	278.7 ± 172.3	251.0 ± 161.4	0.381
Peak CK-MB (ng/dl)	222.1 ± 123.5	193.7 ± 123.5	250.6 ± 117.7	0.014
Peak hs-cTnT (ng/ml)	6.39 ± 3.78	5.33 ± 3.34	7.45 ± 3.93	0.003
Creatinine (mg/dl)	1.00 ± 0.19	1.02 ± 0.18	0.97 ± 0.19	0.181
MPV (fl)	7.58 ± 1.16	6.77 ± 0.32	8.39 ± 1.13	<0.001
Baseline hsCRP (mg/dl)	1.60 ± 2.25	1.70 ± 2.35	1.50 ± 2.17	0.647
Peak hsCRP (mg/dl)	3.32 ± 4.43	3.03 ± 4.46	3.61 ± 4.41	0.488
Angiographic data				
Culprit artery				
LAD (%)	42.9	46.4	39.3	0.445
LCx (%)	14.3	12.5	16.1	0.589
RCA (%)	42.9	41.1	44.6	0.703
Multivessel disease (%)	56.3	48.2	64.3	0.086
Baseline TIMI flow grade 0–1 (%)	79.5	73.2	85.7	0.102
Final TIMI flow grade 3 (%)	92.0	91.1	92.9	0.728
Angiographic no-reflow (%)	2.7	1.8	3.6	0.558
Thrombus aspiration (%)	23.2	21.4	50.0	0.654
Bare-metal stents (%)	24.1	16.1	32.1	0.047
Stent diameter at culprit artery (mm)	3.13 ± 0.59	3.09 ± 0.55	3.17 ± 0.64	0.488
Stent length at culprit artery (mm)	31.5 ± 18.0	31.4 ± 17.4	31.5 ± 18.9	0.988
Glycoprotein IIb/IIIa inhibitor (%)	57.1	46.4	67.9	0.022
CE-CMR imaging data				
LVEDV (ml)	140.1 ± 32.9	136.1 ± 29.6	144.1 ± 35.7	0.202
LVESV (ml)	70.4 ± 28.8	63.8 ± 18.6	77.0 ± 35.2	0.015
LV mass (g)	89.1 ± 16.2	86.9 ± 14.2	91.6 ± 17.8	0.124
LV EF (%)	49.8 ± 9.8	53.0 ± 8.1	46.7 ± 10.4	0.001
Infarct size, % of LV	6.88 ± 5.5	5.54 ± 4.7	8.22 ± 5.9	0.009
AAR, % of LV	17.4 ± 11.1	18.2 ± 12.1	16.6 ± 10.1	0.470
Myocardial salvage index (%)	0.58 ± 0.26	0.66 ± 0.25	0.51 ± 0.25	0.003
Hemorrhagic infarction (%)	0.57 ± 1.27	0.51 ± 1.38	0.64 ± 1.16	0.607
MVO area, % of LV	0.24 ± 0.55	0.15 ± 0.40	0.34 ± 0.65	0.078
Number of segments with >75% of infarct transmural	1.45 ± 1.73	0.71 ± 1.26	2.20 ± 1.82	<0.001
Maximal infarct transmural (%)	66.0 ± 29.0	55.9 ± 29.6	76.0 ± 24.7	<0.001
Frequency of transmural extent of infarction (%)	46.4	26.8	66.1	<0.001

^a“Smoking” means active smokers as well as ex-smokers who stopped smoking less than 1 year before enrollment.

hsCRP, high sensitivity CRP; PCI, percutaneous coronary intervention; SBP, systolic blood pressure; CK, creatine kinase; hs-cTnT, high-sensitivity cardiac troponin T; LAD, left anterior descending coronary artery; LCX, left circumflex coronary artery; RCA, right coronary artery; TIMI, thrombolysis in myocardial infarction; CE-CMR, contrast-enhanced cardiac magnetic resonance; LV, left ventricle; LVEDV, left ventricular end-diastolic volume; LVESV, left ventricular end-systolic volume; MVO, microvascular obstruction.

Fig. 4. Comparison of receiver operating characteristic curves for peak high-sensitivity CRP level, MPV, creatine kinase-MB, and high-sensitivity cardiac troponin T level for predicting transmural infarction.

was higher and door-to-balloon time was lower in patients with high MPV than in those with low MPV, these trends were not statistically significant. Peak CK-MB and hs-cTnT levels were higher in patients with high MPV than in those with low MPV.

Patients in the high MPV group had longer intervals from the procedure to CE-CMR imaging than those in the low MPV group (58.7 ± 62.7 vs. 43.1 ± 29.3 days, $P = 0.095$). CE-CMR imaging findings are presented in Table 2. LVESV, infarct size, number of segments with $>75\%$ of infarct transmural, and maximal infarct transmural were higher in the high MPV group than in the low MPV group on CE-CMR imaging. In addition, LVEF and myocardial salvage index were lower, and transmural extent of infarction was detected more frequently in the high peak hsCRP level group than in the low peak hsCRP level group. Patients in the high peak hsCRP group had larger MVO area than those in the low peak hsCRP group, and no significant differences were observed in LVEDV, LV mass index, AAR, and hemorrhagic infarction incidence between the two groups.

Comparison of Predictive Values of Peak Cardiac Enzyme Levels, Peak hsCRP Level, and MPV for Transmural Extent of Infarction

ROC curve analysis revealed a cut-off value of 156 ng/dl for CK-MB, with 88.5% sensitivity (95% CI: 76.6–95.6) and 45% specificity (95% CI: 32.1–58.4; AUC = 0.680, $P = 0.0004$), and 4.42 ng/dl for hs-cTnT, with 88.5% sensitivity (95% CI: 76.6–95.6) and 51.7% specificity (95% CI: 38.4–67.8; AUC = 0.696, $P = 0.0001$), for transmural extent of infarction detection (Fig. 4). Z-statistics for comparing individual ROC curves between peak hsCRP level, MPV, and peak cardiac enzyme levels were not significantly different (Fig. 4).

Independent Predictors of Transmural Extent of Infarction

Univariate analysis showed that peak hsCRP level (≥ 2.35 mg/dl), MPV (≥ 7.3 fl), peak CK-MB level (≥ 156 ng/dl), peak hs-cTnT level (≥ 4.42 ng/dl), low baseline

TABLE 3. Univariate and Multivariate Logistic Regression Analyses Determining the Significant and Independent Predictors for Transmural Extent of Infarction, Respectively

Factor	Univariate OR (95% CI), <i>P</i> -value	Multivariate OR (95% CI), <i>P</i> -value
Peak hsCRP (≥ 2.35 mg/dl)	6.18 (2.71–14.17), <0.001	5.16 (1.84–14.50), 0.002
MPV (≥ 7.3 fl)	5.32 (2.37–11.96), <0.001	5.42 (2.03–14.47), 0.001
Peak CK-MB (≥ 156 ng/dl)	5.86 (2.17–15.81), <0.001	2.90 (0.68–12.37), 0.151
Peak hs-cTnT (≥ 4.42 ng/dl)	7.67 (2.85–20.63), <0.001	1.57 (0.37–6.73), 0.542
Baseline low TIMI flow grade (0–1)	4.03 (1.38–11.80), 0.011	1.10 (0.25–4.78), 0.899
Low LVEF ($<55\%$)	6.71 (2.49–18.06), <0.001	1.97 (0.56–6.96), 0.294

Reference group was as follows: Peak hsCRP (<2.35 mg/dl), MPV (<7.3 fl), peak CK-MB (<156 ng/dl), peak hs-cTnT (<4.42 ng/dl), baseline low TIMI flow grade (2, 3), and high LVEF ($\geq 55\%$). Each level was cut-off value for transmural extent of infarction by ROC analysis (except TIMI flow grade).

TIMI flow grade (0 to 1), and low LVEF (<55%) were significantly associated with transmural extent of infarction. Multivariate logistic regression analysis included the significant univariate variables. From this model, the variables found to be independent risk factors of transmural extent of infarction were high peak hsCRP level (≥ 2.35 mg/dl) and high MPV (≥ 7.3 fl; Table 3).

DISCUSSION

To our knowledge, this is the first study to evaluate the relationship between peak hsCRP level/MPV and infarct transmural extent. The main finding was that the high peak hsCRP level and MPV were independent predictors of transmural extent of infarction in patients with STEMI. After adjusting for peak CK-MB level, peak hs-cTnT level, baseline TIMI flow grade, and LVEF, the odds ratio was significant in the high peak hsCRP level and MPV groups. Furthermore, the predictive power of peak hsCRP level and MPV for transmural involvement was comparable to that of peak CK-MB and hs-cTnT levels.

MI extent is the main determinant of mortality risk and probability of heart failure (32,33). CRP level is elevated in patients with acute coronary syndrome, and is recognized as a significant risk factor for coronary artery disease (22,34). Moreover, admission CRP level is a significant independent predictor of short-term (30 days) mortality (35). During AMI, peak CRP concentration measured at 24–72 hr following symptom onset is now recognized as a prognostic indicator of 1-year outcomes (21,22). Evidence of the role of CRP in predicting the extent of myocardial tissue damage in AMI has been found in infarction models with endogenous and exogenous augmented CRP levels (36,37). Recently, some authors have reported that selective CRP apheresis significantly reduces CRP levels and the volume of the infarction zone in a pig model for AMI (38,39).

Platelets are a major cause of atherosclerotic lesions, plaque destabilization, and atherothrombosis (40–43). MPV is an easily evaluable parameter for determining platelet reactivity, and is suggested as a risk factor for overall vascular mortality, such as MI (44). Numerous investigations have demonstrated poor prognoses after acute coronary syndrome in patients with high MPV and an association between MPV and sluggish coronary stream and microvascular injury (45–47).

CE-CMR imaging is a sensitive and reliable technique for identifying the morphological and functional complications of AMI, and has considerable potential as a method of risk stratification and direct management after AMI. CE-CMR imaging can discriminate viable myocardium from infarcted myocardium and can establish transmural extent precisely after MI. Transmurality of infarction is vital to predicting the progress of LV remodeling,

alterations of LV function, and clinical prognoses (27,48–51). The majority of these studies using delayed enhanced imaging showed an inverse association between the transmural degree of delayed enhancement (>75%) and improvement of LV regional contractile function and minimal or no improvement in dysfunctional segments (52).

Recently, the relationship between MPV and infarct size (percentage with respect to the total myocardial mass) in STEMI patients was reported (53). There are no reports of a significant association between peak hsCRP level or MPV and infarct transmural extent in STEMI patients who underwent primary PCI. To our knowledge, this is the first study to report the significant predictive values of peak hsCRP and MPV as biomarkers for transmural extent of infarction in patients with STEMI.

This study was limited by the relatively small sample size. In addition, it was not a prospective study. Consequently, the outcomes and conclusions are subject to the limitations inherent to this type of investigation.

We cannot exclude the possibility of a selection bias in the present study because of the original inclusion criteria used (STEMI patients in whom hsCRP level, MPV, and infarct transmural extent were measured using CE-CMR imaging).

In conclusion, high peak hsCRP level and MPV were found to be independent predictors of transmural extent of infarction in STEMI patients. This predictive power for transmural involvement was independent of peak CK-MB level, peak hs-cTnT level, baseline TIMI flow grade, and LVEF. Moreover, it was comparable to that of peak CK-MB and hs-cTnT levels.

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