Original Article

CMJ

www.cmj.ac.kr

Platelet Reactivity Was Not Associated with Infarct Size after Primary Percutaneous Coronary Intervention

Seohwa Park, Kyeong Ho Yun*, Jae Young Cho, and Seung-Yul Lee

Department of Cardiovascular Medicine, Regional Cardiocerebrovascular Center, Wonkwang University Hospital, Iksan, Korea

Potent antiplatelet therapy after primary percutaneous coronary intervention (PCI) has the potential to reduce infarct size. This study analyzed the association between on-treatment platelet reactivity and myocardial infarct size in patients with ST-segment elevation myocardial infarction (STEMI) undergoing primary PCI. In this single-center, retrospective study, 253 patients who underwent primary PCI for STEMI were divided into two groups according to platelet reactivity measurements (53 patients in the high platelet reactivity [HPR] group and 200 in the non-HPR group). Technetium Tc-99m tetrofosmin single-photon emission computed tomography (SPECT) was performed before hospital discharge. We measured the infarct size using SPECT imaging and serial cardiac biomarker levels, and compared the infarct sizes of each group. The patients with HPR were older (65.5±13.2 vs. 60.6±12.1 years, p=0.011) than the patients with non-HPR. On the other hand, the non-HPR group had a higher incidence of smoking (26.4% vs. 51.0%, p=0.001) than the HPR group. Infarct size was similar between the two groups (22.6±17.3% vs. 24.8±17.7%, p=0.416). Multivariate analysis revealed that onset to balloon time >240 min (odds ratio [OR]=1.92; 95% confidence interval [CI]=1.08-3.40; p=0.025) and anterior infarction (OR=5.28; 95% CI=3.05-9.14; p<0.001) were independent predictors of large (>22%) infarct size. HPR was not a predictor of infarct size assessed by SPECT. The two groups also showed analogous cumulative creatinine kinase-myocardial band and troponin T levels. In conclusion, compared to non-HPR, HPR showed no significant association with myocardial infarct size measured by SPECT imaging in early phase of MI.

Key Words: *Angioplasty; Myocardial Infarction; Blood Platelets; P2Y12 receptors*

Article History:
Received June 7, 2021
Revised June 22, 2021
Accepted June 23, 2021

Corresponding Author:
Kyeong Ho Yun
Department of Cardiovascular Medicine, Regional Cardiocerebrovascular Center, Wonkwang University Hospital, 895 Muwang-ro, Iksan 54538, Korea
Tel: +82-63-859-2524
Fax: +82-63-852-8480
E-mail: dryunkh@gmail.com

INTRODUCTION

Acute ST-segment elevation myocardial infarction (STEMI) is one of the largest causes of death worldwide. Mortality and morbidity following STEMI is highly associated with infarct size. Large infarct size increases the risk of symptomatic heart failure and cardiac death.[1-4] One study demonstrated that patients with an infarction >12% of the left ventricle showed a 7% mortality rate at 2 years, while those with an infarction <12% had 0% mortality.[5] Thus, optimizing the strategy to minimize infarct size is essential to STEMI management.

Prompt revascularization is the cornerstone to treating STEMI patients. In addition to primary percutaneous coronary intervention (PCI), various antiplatelet therapies have been applied in acute MI treatment. These antiplatelet agents play a potential role in reducing infarct size, as they affect the no-reflow phenomenon and microvascular obstruction which are associated with embolization of particles during primary PCI.[6,7] Studies using antiplatelet agents demonstrated that newer agents such as ticagrelor and prasugrel had greater reduction effects of infarct size than clopidogrel.[8-10] However, other research has also reported conflicting evidence.[11]

Therefore, we hypothesized that platelet reactivity after antiplatelet treatment could be associated with infarct size. We retrospectively analyzed the connection between on-treatment platelet reactivity and myocardial infarct

https://doi.org/10.4068/cmj.2021.57.3.204

size estimated by technetium Tc-99m tetrafosmin single-photon emission computed tomography (SPECT) in STEMI patients treated with primary PCI.

MATERIALS AND METHODS

1. Study population

The present study was a single-center, retrospective, cohort analysis. From February 2015 to March 2019, consecutive patients who were treated with primary PCI for STEMI were enrolled as the study participants. We recruited eligible patients of at least 20 years of age, who, within 24 hours of symptom onset, showed documented ischemia with significant lesions in a native coronary artery. Exclusion criteria included lack of platelet reactivity and SPECT data, need for oral anticoagulation therapy, platelet glycoprotein IIb/IIIa inhibitors, and previous medication with P2Y12 receptor blockers. A detailed study flow is presented in Fig. 1.

Risk factors, such as the following were recorded: previous history of hypertension or current antihypertensive therapy treatment, diabetes treated with insulin or oral antihyperglycemic agent or baseline HbA1c >6.5%, and any type of smoking experience in the last 1 month. All patients provided informed consent for processing their anonymous data, according to a protocol approved by the Institutional Review Board of Wonkwang University Hospital (2019-04-004).

Eligible patients received echocardiography and SPECT imaging before hospital discharge. All patients received a 30-day clinical follow-up and echocardiographic examination 30 days after PCI.

2. Percutaneous coronary intervention

Aspirin (300 mg/day) was administered to all patients before the PCI procedure. A P2Y12 inhibitor, clopidogrel (300 mg) or ticagrelor (180 mg) was also loaded according to the operator's preference. An intravenous bolus of 5,000 U of unfractionated heparin was injected, and then additional heparin boluses were administered to maintain activated clotting time >300 s during the procedure. Standard interventional techniques with second generation drug-eluting stents were used to perform coronary angiography and stent implantation. After the procedure, all of the patients were prescribed aspirin (100 mg/day), clopidogrel (75 mg/day) or ticagrelor (180 mg/day) and statins.

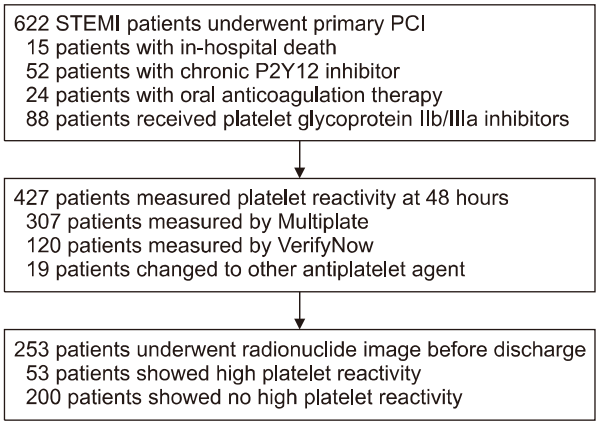

FIG. 1. Flow chart of entire study. STEMI: ST-segment elevation myocardial infarction, PCI: percutaneous coronary intervention.

3. Platelet reactivity assessment

Blood samples were obtained from patients 48 hours after PCI for platelet function testing. Multiple electrode platelet aggregometry (Multiplate analyzer, Roche Diagnostics GmbH, Mannheim, Germany) or VerifyNow (Accumetrics, CA, USA) was used to assess platelet reactivity. High on-treatment platelet reactivity (HPR) was defined as $\geq$47 U for Multiplate analyzer and >208 P2Y12 reaction unit for VerifyNow.[12]

4. Myocardial infarct size

Myocardial infarct size was estimated using SPECT imaging and enzymatic measurements. Creatine kinase myocardial band (CK-MB) isoenzyme and cardiac troponin T were measured before and 8, 24, and 48 hours after primary PCI. Peak concentrations were distinguished, and the time-concentration curve zone was defined using cardiac biomarker levels measured at individual time-points.[13]

SPECT imaging with technetium Tc-99m tetrofosmin was performed according to a standardized technique.[14,15] After administering adenosine, 370 MBq of technetium Tc-99m tetrofosmin was injected intravenously to obtain stress myocardial images. After 4 hours, another 1110 MBq of technetium Tc-99m tetrofosmin was injected intravenously to acquire rest myocardial images. SPECT imaging was performed with a dual-headed gamma camera (Vertex 60, Philips ADAC, USA) equipped with high-resolution collimators. A specialist, with no previous knowledge of the patients' groups, quantified the size of infarction and expressed it in percentages regarding the involvement of the left ventricle. Ejection fraction, summed motion score, and summed thickening score were estimated using automatic method.

5. Study end points

The primary end point was myocardial infarct size, as assessed by SPECT imaging. The secondary end points included (1) infarct size estimated by serial cardiac biomarker measurements, (2) composite outcomes in 30-day clinical trials of all-cause mortality, recurrent myocardial infarction, ischemic stroke, any type of revascularization, and re-hospitalization for congestive heart failure, and (3) in-hospital and 30-day echocardiographic parameters including ejection fraction and wall motion score index.

6. Statistical analysis

All measurements were represented as mean±standard deviation or absolute number (percentage). Inter-group analysis was performed using independent t-test, χ^2 test,

and Fischer's exact test, which were conducted using SPSS 26.0 for Window (SPSS Inc., Chicago, IL). Infarct size, according to the tirtile of platelet reactivity, was compared by ANOVA test. A multivariable logistic regression model was constructed to predict large infarct size (greater than median value, >22%). The following variables selected according to significant univariate analysis were inserted into the logistic regression analysis: onset to balloon time, anterior MI, and final thrombolysis in myocardial infarction (TIMI) flow grade. Statistical significance was set at $p< 0.05$.

RESULTS

1. Baseline characteristics

HPR was shown in 20.9% of patients at 48 hours. Table 1 displays the baseline clinical characteristics of the patients in both groups. Patients with HPR were older (65.5±13.2 vs. 60.6±12.1 years, p=0.011) than patients with non-HPR, while the non-HPR group had higher incidence of smokers (26.4% vs. 51.0%, p=0.001) than the HPR group. Compared to the non-HPR group, the HPR group showed a higher rate of female gender, diabetes, and previous ischemic stroke. However, these were not statistically significant. Other risk factors like onset-to-balloon time and baseline laboratory findings were analogous between the two groups.

The two groups showed similar angiographic and procedural characteristics (Table 2). The HPR group had higher incidences of clopidogrel pretreatment than the non-HPR group (90.6% vs. 27.0%, p<0.001). However, regarding the incidence of slow/no-reflow and final TIMI flow grades, the two groups displayed similar results.

2. Primary endpoint

The SPECT imaging was obtained at a mean of 2.4±1.1 days (interquartile range, 2-3 days) after PCI. The median infarct size assessed by SPECT was 22.0% (interquartile range, 10.0-37.0%). There was no difference in infarct size between the patients treated with clopidogrel and those with ticagrelor (24.4±18.0 vs. 24.3±17.4%, p=0.961). Moreover, Infarct size did not differ significantly with the tirtile of platelet reactivity (Fig. 2). Infarct size was 24.5±17.6%, 28.8±17.7, 23.7±18.8% from 1st to 3rd tirtile of platelet reactivity by mutiplate analyzer (p=0.267), and 18.9±14.8%, 23.8±18.0%, 21.0±15.5% by VerifyNow (p=0.557), respectively. Moreover, the two groups had analogous mean myocardial infarct size (22.6±17.3% vs. 24.8±17.7%, p=0.416) (Table 3). No differences were discovered in the ejection fraction, summed motion score, and summed thickening score. The same results only occurred when anterior MI patients were analyzed (28.7±20.4 in HPR vs. 33.6±17.7% in non HPR, p=0.222).

TABLE 1. Baseline clinical characteristics

	HPR (n=53)	Non-HPR (n=200)	p-value
Age (years)	65.5±13.2	60.6±12.1	0.011
Male (%)	36 (67.9)	160 (80.0)	0.061
Body mass index (kg/m^2)	23.3±3.3	24.3±3.5	0.056
Hypertension (%)	24 (45.3)	94 (47.0)	0.824
Diabetes (%)	14 (26.4)	31 (15.5)	0.065
Current smoker (%)	14 (26.4)	102 (51.0)	0.001
Prior ischemic stroke (%)	5 (9.4)	6 (3.0)	0.056
Anterior infarction (%)	27 (50.9)	100 (50.0)	0.903
Killip class ≥2 (%)	8 (15.1)	31 (15.5)	0.942
Door-to-balloon time (min)	74±12	68±5	0.599
Onset-to-door time (min)	289±33	285±19	0.923
Baseline laboratory findings			
Platelet (×10^3/μL)	250.4±78.8	233.9±51.5	0.155
Serum creatinine (mg/dL)	0.96±0.30	1.03±0.68	0.463
Troponin T (ng/mL)	0.52±1.43	0.60±2.52	0.835
LDL cholesterol (mg/dL)	117.0±34.1	117.1±42.2	0.990
hsCRP (mg/L)	8.4±26.5	5.7±22.0	0.463
BNP (pg/mL)	167.0±319.7	114.1±280.1	0.267
Medications after procedure (%)			
Aspirin	53 (100)	198 (99.0)	1.000
ACE inhibitor	34 (64.2)	139 (69.5)	0.457
ARB	16 (30.2)	49 (24.5)	0.399
Beta blocker	41 (77.4)	170 (85.0)	0.184
Statin	53 (100)	196 (98.0)	0.582

CKMB: creatine kinase myocardial band isoenzyme, LDL: low density lipoprotein, hsCRP: high-sensitivity C-reactive protein, ACE: angiotensin converting enzyme, ARB: angiotensin receptor blocker.

TABLE 2. Coronary angiographic and procedural characteristics

	HPR (n=53)	Non-HPR (n=200)	p-value
Culprit lesion (%)			0.388
Left main	0 (0.0)	3 (1.5)	
Left anterior descending	27 (50.9)	97 (48.5)	
Left circumflex	10 (18.9)	24 (12.0)	
Right coronary artery	16 (30.2)	76 (38.0)	
Multivessel disease (%)	16 (30.2)	67 (33.5)	0.648
Pretreatment (%)			<0.001
Clopidogrel	48 (90.6)	54 (27.0)	
Ticagrelor	5 (9.4)	146 (73.0)	
Thrombus aspiration (%)	8 (15.1)	22 (11.0)	0.412
Multivessel PCI (%)	4 (7.5)	11 (5.5)	0.525
Stent number per patient	1.1±0.4	1.2±0.5	0.406
Stent diameter (mm)	3.0±0.4	3.1±0.4	0.205
Total stent length (mm)	29.1±13.6	32.1±14.8	0.184
Maximal pressure (atm)	14.6±3.5	14.5±3.0	0.841
Baseline TIMI flow grade 0/1 (%)	41 (77.4)	180 (90.0)	0.014
Final TIMI flow grade <3 (%)	3 (5.7)	5 (2.5)	0.370
Procedural complications (%)	6 (11.3)	22 (11.0)	0.947
Slow/no reflow	2 (3.8)	8 (4.0)	1.000
Distal embolization	3 (5.7)	12 (6.0)	1.000
Side branch occlusion	1 (1.9)	4 (2.0)	1.000

PCI: percutaneous coronary intervention, TIMI: thrombolysis in myocardial infarction.

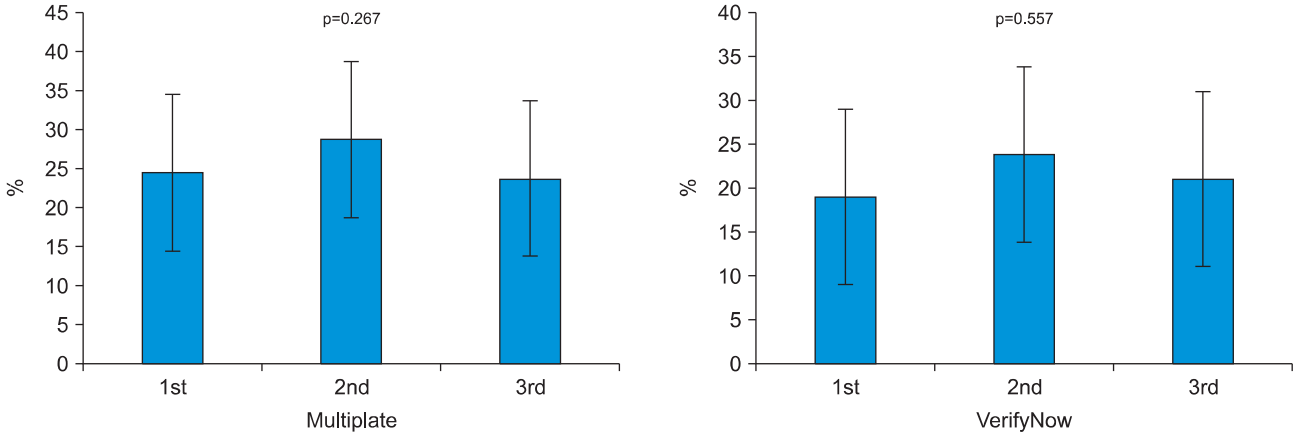

FIG. 2. Infarct size according to the tirtile of platelet reactivity.

TABLE 3. Radionuclide imaging and enzymatic infarct size

	HPR (n=53)	Non-HPR (n=200)	p-value
SPECT results			
Infarct size (%)	22.6±17.3	24.8±17.7	0.416
Summed motion score	19.9±16.7	21.1±16.5	0.655
Summed thickening score	14.2±11.2	15.4±10.6	0.448
End-diastolic volume (mL)	102.5±48.2	113.9±35.3	0.056
End-systolic volume (mL)	55.1±42.3	61.7±30.2	0.198
Ejection fraction (%)	50.5±12.3	48.2±11.3	0.204
Biomarker results (ng/mL)			
CK-MB at baseline	11.1±17.2	23.2±59.0	0.013
CK-MB at 8 hours	179.5±154.7	238.5±160.8	0.017
CK-MB at 24 hours	59.6±60.6	125.1±532.1	0.373
CK-MB at 48 hours	11.7±9.7	11.9±7.0	0.854
Troponin T at baseline	0.52±1.43	0.60±2.52	0.835
Troponin T at 8 hours	7.09±6.43	8.73±10.25	0.270
Troponin T at 24 hours	4.33±4.26	5.54±16.02	0.584
Troponin T at 48 hours	3.21±2.87	3.55±3.70	0.531

SPECT: technetium Tc-99m tetrofosmin single-photon emission computed tomography, CKMB: creatine kinase myocardial band isoenzyme.

Multivariate analysis revealed that onset to balloon time >240min (odds ratio [OR]=1.92; 95% confidence interval [CI]=1.08-3.40; p=0.025) and anterior infarction (OR=5.28; 95% CI=3.05-9.14; p<0.001) were independent predictors of large (>22%) infarct size (Table 4). HPR was not a predictor of infarct size estimated by SPECT.

3. Secondary endpoint

Initial and peak level of CK-MB was lower in the HPR group; however, the cumulative CK-MB level was similar between the two groups (Fig. 3). At all time-points after PCI (8, 24, and 48 hours), and peak level of troponin T were also similar between the two groups.

There was no difference regarding the ejection fraction and wall motion score index at 30 days (Table 5). The incidence of 30-day clinical events including death, revascularization and re-hospitalization for congestive heart failure were also analogous between the two groups (3.8% vs. 3.0%, p=0.676).

DISCUSSION

In this study, platelet reactivity was not associated with infarct size when assessed by SPECT and cardiac biomarkers in STEMI patients. Moreover, patients in the HPR and non-HPR groups showed similar ejection fractions and wall motion scores at 30 days.

Various antiplatelet agents were evaluated for their potential role in infarct size reduction. Although a small retrospective study failed to demonstrate the reduction of infarct size, ticagrelor was a promising agent for infarct size reduction.[11] Park et al.[16] stated that ticagrelor improved microvascular injury which was measured by index of microcirculatory resistance, and also reduced infarct size measured by cardiac biomarker assay in STEMI patients. Kim et al.[9] reported that myocardial infarct size was found to be significantly smaller in the ticagrelor group than the clopidogrel group of STEMI patients who received primary PCI. The sub-analysis of Complete Versus Lesion-Only PRImary PCI (CvLPRIT) trial and DANish trial in Acute Myocardial Infarction (DANAMI-3) trial also demonstrated a significant reduction of infarct size in ticagrelor, in comparison to clopidogrel pretreatment.[8,10] Moreover, Park et al.[17] reported that ticagrelor was superior to clopidogrel for left ventricular remodeling after reperfusion of STEMI with primary PCI.

Even though ticagrelor treatment showed low incidence of HRP, our results demonstrated that both HPR and non-HPR groups had similar infarct size. However, interpretation of these results should be done cautiously. First, the strong impact of infarct location and onset to balloon time on infarct size could have obscured the role of antiplatelet agent or platelet reactivity in this study. Additional future research is necessary to resolve such problem. Second, the degree of platelet inhibition does not completely reflect the effects of antiplatelet agents. One animal

Table 4. Univariate and multivariate analysis for the prediction of >22% infarct size

	Univariate analysis			Multivariate analysis		
	OR	95% CI	p	OR	95% CI	p
Age >65 years	1.46	0.88-2.43	0.146			
Door-to-balloon time >60 min	1.13	0.67-1.89	0.645			
Onset-to-balloon time >240 min	1.77	1.05-2.97	0.031	1.92	1.08-3.40	0.025
Hypertension	1.41	0.86-2.31	0.176			
Current smoker	1.43	0.87-2.35	0.158			
Anterior infarction	5.05	2.96-8.61	<0.001	5.28	3.05-9.14	<0.001
Multivessel disease	1.18	0.70-2.00	0.529			
Clopidogrel treatment	1.17	0.71-1.94	0.537			
Final TIMI flow grade <3	7.78	0.94-64.22	0.057	7.39	0.83-65.26	0.074
High platelet reactivity	1.18	0.65-2.18	0.585			

For continuous variables, the median value was used as a cut-off point.

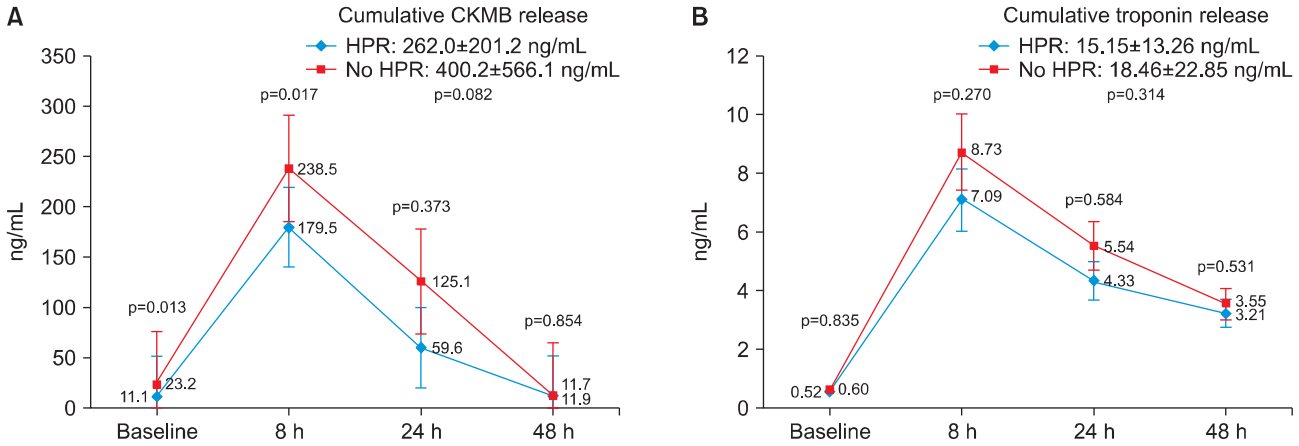

Fig. 3. Time-concentration curve of (A) creatine kinase myocardial band (CKMB) isoenzyme and (B) troponin T.

Table 5. 30-day clinical outcomes and echocardiographic parameters

	HPR (n=53)	Non-HPR (n=200)	p-value
Echocardiography			
Baseline ejection fraction (%)	47.8±8.9	48.0±8.0	0.903
Baseline wall motion score index	1.56±0.35	1.57±0.36	0.847
30-day ejection fraction (%)	53.0±8.5	50.8±8.7	0.102
30-day wall motion score index	1.33±0.31	1.36±0.33	0.526
30-day clinical outcomes			
All-cause death	0 (0.0)	0 (0.0)	
Myocardial infarction	0 (0.0)	0 (0.0)	
Ischemic stroke	0 (0.0)	1 (0.5)	1.000
Stent thrombosis	0 (0.0)	0 (0.0)	
Re-hospitalization for heart failure	1 (1.9)	3 (1.5)	1.000
Total	2 (3.8)	6 (3.0)	0.676

study demonstrated that in comparison to clopidogrel, ticagrelor significantly reduced infarct size assessed by cardiac magnetic resonance imaging (MRI).[18] The study also illustrated that the effects of ticagrelor such as reducing necrotic injury and edema formation, resulted from an adenosine-dependent mechanism. Ticagrelor is also thought to have potential protective effects against ischemia-reperfusion injury which is mediated by adenosine, particularly at sites of ischemia and tissue injury.[19] Therefore, the number of P2Y12 reaction units is not an indicator for complete antiplatelet status. Finally, platelet reactivity can change. Yun et al.[20] reported that the responder status of 43% of patients was altered in the clopidogrel, and 13% in the ticagrelor, which indicates that a single-time point measurement of platelet function may be insufficient for representing platelet reactivity. Moreover, platelet reactivity just before or after PCI would be more predictive of infarct size compared to 48 hours post-procedural platelet reactivity.

Our study has several limitations. We measured the infarct size by SPECT. Currently, however, cardiac MRI is used to assess infarct size, as it provides superior resolution while detecting subendocardial infarction and microvascular obstruction. Nevertheless, in previous studies, the correlation between infarct size measured by SPECT and MRI was good and the prognostic significance was analogous between the two methods in STEMI patients.[21,22]

Another limitation of our study is that the imaging was performed within a period early after MI. Early SPECT imaging between 18 and 48 hours after the event often overestimates the infarct size, which is presumably due to biochemical stunning of the myocardium, limiting isotope uptake.[23] Also, we did not perform baseline SPECT. The difference between baseline and follow-up infarct size could be a better variable. Finally, this was a single center study and the sample size in the HPR group could be too small to demonstrate increased infarct size.

In conclusion, through a small study of STEMI patients treated with primary PCI, we discovered that platelet reactivity was not associated with infarct size which was measured by SPECT during the first 48 hours. Future studies that include a larger number of participants and use better assessment methods for infarct size and clinical outcome evaluations are necessary.

CONFLICT OF INTEREST STATEMENT

None declared.

REFERENCES

1. Stone GW, Selker HP, Thiele H, Patel MR, Udelson JE, Ohman EM, et al. Relationship between infarct size and outcomes following primary PCI: patient-level analysis from 10 randomized trials. J Am Coll Cardiol 2016;67:1674-83.
2. Petriz JL, Gomes BF, Rua BS, Azevedo CF, Hadlich MS, Mussi HT, et al. Assessment of myocardial infarction by cardiac magnetic resonance imaging and long-term mortality. Arq Bras Cardiol 2015;104:159-68.
3. Herlitz J, Hjalmarson A, Lomsky M, Wiklund I. The relationship between infarct size and mortality and morbidity during short-term and long-term follow-up after acute myocardial infarction. Am Heart J 1988;116(5 Pt 1):1378-82.
4. Burns RJ, Gibbons RJ, Yi Q, Roberts RS, Miller TD, Schaer GL, et al. The relationships of left ventricular ejection fraction, end-systolic volume index and infarct size to six-month mortality after hospital discharge following myocardial infarction treated by thrombolysis. J Am Coll Cardiol 2002;39:30-6.
5. Miller TD, Christian TF, Hodge DO, Hopfenspirger MR, Gersh BJ, Gibbons RJ. Comparison of acute myocardial infarct size to two-year mortality in patients <65 to those > or =65 years of age. Am J Cardiol 1999;84:1170-5.
6. Parviz Y, Vijayan S, Lavi S. A review of strategies for infarct size reduction during acute myocardial infarction. Cardiovasc Revasc Med 2017;18:374-83.
7. McAlindon E, Bucciarelli-Ducci C, Suleiman MS, Baumbach A. Infarct size reduction in acute myocardial infarction. Heart 2015; 101:155-60.
8. Sabbah M, Nepper-Christensen L, Køber L, Høfsten DE, Ahtarovski KA, Göransson C, et al. Infarct size following loading with Ticagrelor/Prasugrel versus Clopidogrel in ST-segment elevation myocardial infarction. Int J Cardiol 2020;314:7-12.
9. Kim EK, Park TK, Yang JH, Song YB, Choi JH, Choi SH, et al. Ticagrelor versus clopidogrel on myocardial infarct size in patients undergoing primary percutaneous coronary intervention. J Am Coll Cardiol 2017;69:2098-9.
10. Khan JN, Greenwood JP, Nazir SA, Lai FY, Dalby M, Curzen N, et al. Infarct size following treatment with second- versus third-generation P2Y12 antagonists in patients with multivessel coronary disease at ST-segment elevation myocardial infarction in the CvLPRIT study. J Am Heart Assoc 2016;5:e003403.
11. Yun KH, Rhee SJ, Ko JS. Comparison of the infarct size between the loading of ticagrelor and clopidogrel in patients with acute myocardial infarction undergoing primary percutaneous coronary intervention. Korean Circ J 2017;47:705-13.
12. Tantry US, Bonello L, Aradi D, Price MJ, Jeong YH, Angiolillo DJ, et al. Consensus and update on the definition of on-treatment platelet reactivity to adenosine diphosphate associated with ischemia and bleeding. J Am Coll Cardiol 2013;62:2261-73.
13. Turer AT, Mahaffey KW, Gallup D, Weaver WD, Christenson RH, Every NR, et al. Enzyme estimates of infarct size correlate with functional and clinical outcomes in the setting of ST-segment elevation myocardial infarction. Curr Control Trials Cardiovasc Med 2005;6:12.
14. Hahn JY, Kim HJ, Choi YJ, Jo SH, Kim HJ, Lee S, et al. Effects of atorvastatin pretreatment on infarct size in patients with ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention. Am Heart J 2011;162:1026-33.
15. Kim JW, Yun KH, Kim EK, Kim YC, Joe DY, Ko JS, et al. Effect of high dose rosuvastatin loading before primary percutaneous coronary intervention on infarct size in patients with ST-segment elevation myocardial infarction. Korean Circ J 2014;44:76-81.
16. Park SD, Lee MJ, Baek YS, Kwon SW, Shin SH, Woo SI, et al. Randomised trial to compare a protective effect of Clopidogrel Versus TIcagrelor on coronary Microvascular injury in ST-segment Elevation myocardial infarction (CV-TIME trial). EuroIntervention 2016;12:e964-71.
17. Park Y, Koh JS, Lee JH, Park JH, Shin ES, Oh JH, et al. Effect of ticagrelor on left ventricular remodeling in patients with ST-segment elevation myocardial infarction (HEALING-AMI). JACC Cardiovasc Interv 2020;13:2220-34.
18. Vilahur G, Gutiérrez M, Casani L, Varela L, Capdevila A, Pons-Lladó G, et al. Protective effects of ticagrelor on myocardial injury after infarction. Circulation 2016;134:1708-19.
19. Cattaneo M, Schulz R, Nylander S. Adenosine-mediated effects of ticagrelor: evidence and potential clinical relevance. J Am Coll Cardiol 2014;63:2503-9.
20. Yun KH, Cho JY, Rhee SJ, Oh SK. Temporal variability of platelet reactivity in patients treated with clopidogrel or ticagrelor. Korean Circ J 2019;49:1052-61.
21. Lund GK, Stork A, Saeed M, Bansmann MP, Gerken JH, Müller V, et al. Acute myocardial infarction: evaluation with first-pass enhancement and delayed enhancement MR imaging compared with 201Tl SPECT imaging. Radiology 2004;232:49-57.
22. Hadamitzky M, Langhans B, Hausleiter J, Sonne C, Byrne RA, Mehilli J, et al. Prognostic value of late gadolinium enhancement in cardiovascular magnetic resonance imaging after acute ST-elevation myocardial infarction in comparison with single-photon emission tomography using Tc99m-Sestamibi. Eur Heart J Cardiovasc Imaging 2014;15:216-25.

23. Pellikka PA, Behrenbeck T, Verani MS, Mahmarian JJ, Wackers FJ, Gibbons RJ. Serial changes in myocardial perfusion using tomographic technetium-99m-hexakis-2-methoxy-2-methylpropylisonitrile imaging following reperfusion therapy of myocardial infarction. J Nucl Med 1990;31:1269-75.