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Original article

Association between changes in platelet reactivity during elective percutaneous coronary intervention and periprocedural myocardial infarction: A pilot study

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ABSTRACT

Background: High platelet reactivity before percutaneous coronary intervention (PCI) reportedly increases the risk of PCI-related myocardial infarction (PMI) following elective PCI. We conducted a pilot study to evaluate changes in platelet reactivity during PCI and their association with the incidence of PMI.

Methods: In total, 133 consecutive patients undergoing elective PCI after pretreatment with dual antiplatelet therapy for at least 7 days were prospectively enrolled. Platelet reactivity was measured by the VerifyNow® assay (International Technidyne Corporation, Edison, NJ, USA) immediately before and after PCI.

Results: Platelet reactivity significantly increased from 177.3 ± 53.4 P2Y12 reaction units (PRU) before PCI to 203.4 ± 52.8 PRU immediately after PCI ($p < 0.001$). Absolute changes in platelet reactivity were significantly greater in patients with than without PMI (32.4 ± 29.0 vs. 21.2 ± 24.8 PRU, respectively; $p = 0.021$). In the multivariable logistic regression analysis, the absolute change in PRU was an independent predictor of the incidence of PMI. Receiver operating characteristic curve analysis of the change in PRU during PCI for discriminating PMI showed a sensitivity, specificity, and the cut-off value of 46%, 76%, and 37 PRU, respectively (area under the curve = 0.607, $p = 0.0235$). When the patients were divided into two groups, namely a greater (change in PRU ≥ 37) and smaller (change in PRU < 37) increase group, the incidence rate of PMI was significantly higher in the greater than smaller increase group (59.1% vs. 34.8%, respectively; $p = 0.008$). Additional exploratory analyses by intracoronary imaging demonstrated that the proximal reference lumen area in the greater increase group was significantly smaller than that in the smaller increase group (6.5 ± 2.4 vs. 7.7 ± 3.1 mm^2, respectively; $p = 0.032$).

Conclusion: An increase in platelet reactivity after elective PCI is possibly associated with PMI. This finding should be validated by a larger-scale study.

Introduction

Percutaneous coronary intervention (PCI)-related myocardial infarction (PMI) in patients with stable coronary artery disease is reportedly associated with an increased risk of major adverse events [1–3]. A recent report stated that perioperative myocardial injury after non-cardiac surgery, defined as an absolute increase in high-sensitivity cardiac troponin T, is a common complication associated with substantial short- and long-term mortality [4]. Previous studies have shown that the incidence of PMI varies from 5% to 40% according to the diagnostic criteria and local practices [5,6]. The factors influencing the incidence of PMI can be broadly

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classified into patient-related factors, angiographic or lesion-related factors, and procedural factors [5–7].

Dual antiplatelet therapy with aspirin and prasugrel or clopidogrel is commonly used for patients who undergo PCI. Clopidogrel and prasugrel inhibit ADP-induced platelet activation through binding to the platelet P2Y12 ADP receptor after metabolic transformation [8]. High platelet reactivity during clopidogrel treatment is also associated with an increased risk of PMI [9,10]. However, an association between changes in platelet reactivity during PCI and the occurrence of PMI has not been reported. In addition, studies have shown an association between high platelet reactivity and major adverse events in patients undergoing PCI [11–13], but whether changes in platelet reactivity during PCI are associated with adverse events after PCI remains unknown.

Therefore, in this pilot study, we evaluated changes in platelet reactivity during elective PCI in patients treated with prasugrel for a sufficient duration. Furthermore, we investigated the association of such changes with the incidence of cardiac events, including PMI, and potential factors involved in changes in platelet reactivity.

Methods

Patient population and study protocol

We performed a prospective observational study from January 2016 to December 2017. The study was approved by the ethics committees of Okayama University Hospital and Okayama City Hospital. All participants provided written informed consent before enrollment. The study was conducted according to the principles of the Declaration of Helsinki. The study was registered in the UMIN Clinical Trials Registry (UMIN000018437).

Patients with stable angina who underwent elective PCI were prospectively enrolled. The exclusion criteria were a body weight of <50 kg, age of >85 years, bleeding tendency, severely impaired liver function (Child–Pugh classification grade C), severely impaired renal function (estimated glomerular filtration rate of ≤30 ml/min/1.73 m^2), current or past cerebral infarction, uncontrolled hypertension (systolic blood pressure of ≥180 mmHg), or judgment of patient inadequacy for PCI by the attending physician. Patients with no or slow coronary flow (Thrombolysis In Myocardial Infarction 0–2) in target vessels or main branches (≥2-mm vessel diameter) after stent implantation were also excluded. Finally, 133 consecutive patients were analyzed.

All patients underwent dual antiplatelet therapy with prasugrel (3.75 mg daily) and aspirin (100 mg daily) for at least 7 days before PCI. Using the American College of Cardiology/American Heart Association classification, coronary lesions were divided into four groups (types A, B1, B2, and C) based on angiographic findings. The technicalities of the procedure were at the operator's discretion. Heparin was administrated to achieve an activated clotting time of 250–300 s. Pre-dilatation is balloon dilatation before stent placement, and post-dilatation is balloon dilatation at the time of or after stent placement. In the case of multiple stentings, the average stent diameter and sum total stent length were calculated. Procedural success was defined as a reduction of stenosis to <25% residual narrowing.

Definition of PMI

High-sensitivity troponin-T (hs-TnT) was measured before and 24 h after PCI. In patients with a normal baseline hs-TnT concentration (≤99th percentile of the upper reference limit), PMI was defined as elevation of hs-TnT to >5-fold the 99th percentile of the upper reference limit 24 h after PCI. If the baseline hs-TnT value was elevated and stable or falling, then a rise of >20% was required for a diagnosis of PMI [14].

Assessment of platelet reactivity

The response to prasugrel was assessed by the VerifyNow® P2Y12 assay (International Technidyne Corporation, Edison, NJ, USA) according to the manufacturer's instructions [15]. Platelet reactivity is reported in P2Y12 reaction units (PRU) immediately before and after PCI. Blood samples were collected twice per procedure from the artery immediately after sheath placement and immediately before sheath removal after PCI.

Endpoints

The primary outcomes of the study were the change in platelet reactivity during PCI and the correlation between the change in platelet reactivity and the incidence of PMI. The secondary outcome was the correlation between the change in platelet reactivity during PCI and the occurrence of thrombotic or hemorrhagic events 30 days after PCI. Hemorrhagic events were defined as Bleeding Academic Research Consortium (BARC) classification type 3–5 [16]. As exploratory analyses, we investigated the procedural and intracoronary imaging characteristics of patients with a greater increase in platelet reactivity during PCI and with an incidence of PMI.

Risk factors

Hypertension was defined as blood pressure of >140/90 mmHg in repeated measurements or current use of antihypertensive medications. Dyslipidemia was defined as documented hyperlipidemia or use of lipid-lowering medications. Diabetes mellitus was defined as an HbA1c concentration of >6% or use of antihyperglycemic medications. Smoking status was defined as both current and past smoking. Chronic kidney disease was defined as an estimated glomerular filtration rate of <60 ml/min/1.73 m^2.

Angiography, intracoronary ultrasound, and optical frequency domain imaging analysis

A computerized quantitative analysis system was employed with a guiding catheter for calibration. Angiographic measurements included the mean reference diameter, minimum lesion diameter, diameter stenosis, and lesion length. As exploratory analyses, we evaluated associations of the change in platelet reactivity and incidence of PMI with imaging characteristics. Lesion morphology was assessed by intracoronary imaging using either intravascular ultrasound (IVUS) or optical frequency domain imaging (OFDI). Which imaging device to use was at the operator's discretion according to the patient or lesion characteristics.

IVUS studies were performed with a mechanical sector scanner (ViewIT®; Terumo Corporation, Tokyo, Japan) and a motorized transducer pullback system (2 mm/s). OFDI studies were also performed with a mechanical sector scanner (LUNAWAVE®; Terumo Corporation) in combination with a motorized transducer pullback system (40 mm/s) and contrast injection into the coronary artery through a guiding catheter. The external elastic membrane (EEM) cross-sectional area (CSA), and lumen CSA at the proximal and distal reference were measured. The target lesion EEM CSA divided by the average proximal and distal reference EEM CSA was defined as the remodeling index. The total plaque volume was calculated as the sum of plaque plus media in each CSA at 1-mm axial intervals in the IVUS and OFDI images from the target lesion. When more than two consecutive frames were not analyzable because of artifacts or residual blood, the case was considered to have poor image quality and therefore excluded. Incomplete stent apposition was defined as separation of the inner surface of a stent strut from the inner vessel wall in segments

without a side branch. Peri-stent dissection was defined as disruption of the luminal vessel surface within the stented segment. Stent edge dissection was defined as disruption of the vessel luminal surface with a visible flap at the stent edge or 5 mm proximal and distal reference segments.

Statistical analysis

Continuous variables were compared by the *t*-test for normally distributed values. Otherwise, the Mann–Whitney *U*-test was used. Proportions were compared by the chi-square test when the expected frequency was ≥5. Otherwise, Fisher's exact test was applied. For multivariable logistic regression analysis to assess the predictors of PMI, variates with *p*-value of <0.1 in univariable analysis were included. The optimal cut-off value was determined using receiver operating characteristic curve analysis. Results are expressed as the mean ± standard deviation. A two-tailed *p*-value of <0.05 was considered significant. Analyses were performed with JMP® 11 software (SAS Institute Inc., Cary, NC, USA).

Results

Patient population and changes in platelet reactivity during PCI

We performed elective PCI for 197 patients from January 2016 to December 2017. Sixty-four patients were excluded because of severely impaired renal function (13 patients), undergoing dual antiplatelet therapy for <7 days before PCI (7 patients), and undergoing dual antiplatelet therapy with clopidogrel and aspirin for reasons of older age, lower body weight, and bleeding tendency (44 patients). In total, 133 consecutive patients who underwent elective PCI were assessed. The procedural success rate was 100%. No patients had no or slow coronary flow in the target vessels or main branches after stent implantation. All patient characteristics, including coronary risk factors, are shown in Table 1. As shown in Fig. 1, platelet reactivity before PCI in all patients was 177.3 ± 53.4 PRU, and it significantly increased immediately after PCI to 203.4 ± 52.8 PRU ($p < 0.001$).

Correlation between changes in PRU and incidence of PMI

Among the 133 patients, PMI occurred in 57 patients (42.8%). The absolute change in platelet reactivity during PCI was significantly greater in patients with than without PMI (32.4 ± 29.0 PRU vs. 21.2 ± 24.8 PRU, respectively; $p = 0.021$) (Table 2 and Fig. 2A). We compared the baseline, angiographic, procedural, and imaging characteristics between the PMI and non-PMI groups in Table 2. As imaging techniques, IVUS and OFDI were used for 36 and 21 patients, respectively, in the PMI group and for 35 and 41 patients, respectively, in the non-PMI group. Although there was no significant difference between these two groups except in the absolute change in PRU, the total stent length tended to be longer in the PMI than non-PMI group ($p = 0.058$). In the univariable analysis, the absolute change in PRU and the total stent length were significantly correlated with the incidence of PMI; in the multivariable logistic regression analysis, the absolute change in PRU was the only independent predictor of PMI (Table 3). The receiver operating characteristic curve analysis of the change in PRU during PCI for discriminating PMI showed a sensitivity, specificity, and cut-off value of 46%, 76%, and 37 PRU, respectively (area under the curve = 0.607, $p = 0.024$) (Supplement 1). We compared the patient characteristics, including procedural and imaging characteristics, between the greater and smaller increase groups using this cut-off value in Table 4. As imaging techniques, IVUS and OFDI were used for 23 and 21 patients, respectively, in the greater increase group and for 48 and 41 patients, respectively, in the smaller increase group. There was no significant difference in the baseline and angiographic characteristics between these two groups. Among the procedural characteristics, however, the maximum pressure of predilatation was significantly lower in the greater increase group. Furthermore, among the imaging characteristics, the proximal reference lumen area was significantly smaller in the greater increase group than in the smaller increase group (6.5 ± 2.4 mm^2 vs. 7.7 ± 3.1 mm^2, respectively;

Table 1
Baseline patient characteristics, preceding medications, laboratory data and angiographic characteristics ($n = 133$).

Age, y	70.8 ± 10.2
Male	102 (76.7)
Coronary risk factor	
Hypertension	98 (73.7)
Dyslipidemia	95 (71.4)
Diabetes mellitus	72 (54.1)
Smoking	63 (47.4)
Chronic kidney disease	49 (36.8)
Preceding medication	
Calcium-channel blocker	52 (39.1)
β-Blocker	53 (39.8)
RAS-inhibitor	78 (58.6)
Statin	92 (69.2)
Insulin	14 (10.5)
DPP-4 inhibitor	41 (30.8)
Metformin	9 (6.8)
Laboratory data	
LDL-cholesterol, mg/dl	98.9 ± 29.7
HDL-cholesterol, mg/dl	46.5 ± 12.0
Triglyceride, mg/dl	140.3 ± 84.8
HbA1c, %	6.6 ± 1.1
Creatinine, mg/dl	0.9 ± 0.3
eGFR, ml/m/1.73 m^2	64.9 ± 17.4
Angiographic characteristics	
Left anterior descending artery	67 (50.4)
Left circumflex artery	25 (18.8)
Right coronary artery	46 (34.6)
Left main trunk	4 (3.0)
Multivessel disease	25 (18.8)
Type B2 or C	85 (63.9)
In-stent restenosis	7 (5.3)

Data are presented as mean ± standard deviation or number (%). RAS, renin–angiotensin system; DPP, dipeptidyl peptidase; LDL, low-density lipoprotein; HDL, high-density lipoprotein; Hb, hemoglobin; eGFR, estimated glomerular filtration rate.

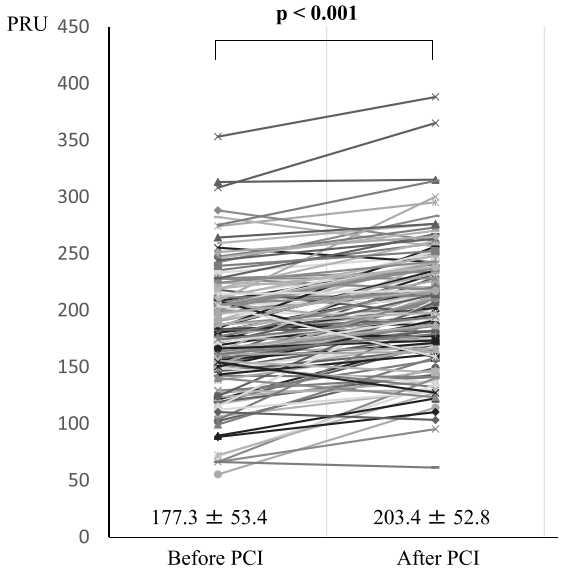

Fig. 1. Changes in platelet reactivity during PCI. PRU, P2Y12 reaction unit; PCI, percutaneous coronary intervention.

Table 2
Baseline, angiographic, procedural, and imaging characteristics of PMI and non-PMI groups.

	PMI group ($n=57$)	Non-PMI group ($n=76$)	p
Age, y	71.6 ± 11.7	70.4 ± 8.9	0.508
Male	41 (71.9)	61 (80.3)	0.261
PRU value before PCI	173.6 ± 55.4	180.1 ± 52.0	0.491
PRU value after PCI	206.0 ± 58.6	201.4 ± 48.3	0.628
Absolute change of PRU value	32.4 ± 29.0	21.2 ± 24.8	0.021
Coronary risk factor			
Hypertension	39 (68.4)	59 (77.6)	0.233
Dyslipidemia	41 (71.9)	54 (71.1)	0.912
Diabetes mellitus	28 (49.1)	44 (57.9)	0.315
Smoking	27 (47.4)	36 (47.4)	1.000
Chronic kidney disease	24 (42.1)	25 (32.9)	0.276
Preceding medication			
Calcium-channel blocker	22 (38.6)	30 (39.5)	0.918
β-Blocker	23 (40.4)	30 (39.5)	0.919
RAS-inhibitor	33 (57.9)	45 (59.2)	0.879
Statin	38 (66.7)	54 (71.1)	0.568
Insulin	5 (8.8)	9 (11.8)	0.534
DPP-4 inhibitor	18 (31.6)	23 (30.3)	0.871
Metformin	3 (5.3)	6 (7.9)	0.732
Laboratory data			
LDL-cholesterol, mg/dl	102.0 ± 30.0	96.1 ± 29.4	0.264
HDL-cholesterol, mg/dl	45.3 ± 11.7	47.2 ± 12.2	0.378
LDL/HDL ratio	2.4 ± 0.9	2.1 ± 0.8	0.085
Triglyceride, mg/dl	133.1 ± 66.0	145.5 ± 97.6	0.390
HbA1c, %	6.6 ± 1.1	6.6 ± 1.1	0.901
Creatinine, mg/dl	0.9 ± 0.3	0.9 ± 0.2	0.576
eGFR, ml/m/1.73 m^2	64.2 ± 20.0	65.6 ± 15.4	0.671
Angiographic characteristics			
Left anterior descending artery	28 (49.1)	39 (51.3)	0.802
Left circumflex artery	12 (21.1)	13 (17.1)	0.564
Right coronary artery	20 (35.1)	26 (34.2)	0.916
Left main trunk	2 (3.5)	2 (2.6)	1.000
Multivessel disease	11 (19.3)	14 (18.4)	0.898
Type B2 or C	38 (66.7)	47 (61.8)	0.566
In-stent restenosis	3 (5.3)	4 (5.3)	1.000
QCA measurements			
Mean reference diameter, mm	2.2 ± 0.5	2.3 ± 0.6	0.301
Minimum lesion diameter, mm	0.7 ± 0.4	0.7 ± 0.4	0.882
Diameter stenosis, %	68.2 ± 16.9	69.5 ± 13.5	0.304
Lesion length, mm	22.2 ± 14.5	17.8 ± 12.5	0.124
Procedural characteristics			
Ad-hoc PCI	19 (33.3)	36 (47.4)	0.104
Procedural duration, min	87.8 ± 44.2	82.2 ± 35.7	0.427
Volume of contrast medium, ml	134.0 ± 42.3	142.3 ± 48.3	0.297
Total number of balloon dilatation	9.5 ± 5.9	7.9 ± 4.7	0.083
Max pressure of predilatation, atm	8.7 ± 3.2	9.1 ± 2.6	0.473
Max pressure of postdilatation, atm	16.5 ± 4.2	15.7 ± 4.1	0.251
Mean stent diameter, mm	2.9 ± 0.5	2.9 ± 0.5	0.953
Total stent length, mm	32.1 ± 17.1	26.5 ± 16.0	0.058
Imaging characteristics			
Calcification (>180°)	20 (35.1)	24 (31.6)	0.670
Proximal reference EEM CSA, mm^2	13.7 ± 4.5	14.3 ± 4.4	0.504
Proximal reference lumen CSA, mm^2	7.4 ± 3.0	7.3 ± 2.9	0.833
Distal reference EEM CSA, mm^2	9.7 ± 3.8	11.1 ± 4.8	0.128
Distal reference lumen CSA, mm^2	6.0 ± 2.8	5.8 ± 3.0	0.701
Minimal stent area, mm^2	5.8 ± 2.1	5.9 ± 2.1	0.825
Incomplete stent apposition	4 (7.0)	12 (15.8)	0.178
Peri-stent dissection	9 (15.8)	7 (9.2)	0.248
Stent edge dissection	1 (1.8)	1 (1.3)	1.000

Data are presented as mean ± standard deviation or number (%). PCI, percutaneous coronary intervention; PMI, PCI-related myocardial infarction; PRU, P2Y12 reaction unit; RAS, renin–angiotensin system; DPP, dipeptidyl peptidase; LDL, low-density lipoprotein; HDL, high-density lipoprotein; Hb, hemoglobin; eGFR, estimated glomerular filtration rate; QCA, quantitative coronary angiography; EEM, external elastic membrane; CSA, cross-sectional area.

$p=0.032$). After the intervention, peri-stent dissection occurred more frequently in the greater than smaller increase group (22.7% vs. 6.7%, respectively; $p=0.008$). Two cases of stent edge dissection occurred in the greater increase group. The minimal stent areas were similar in the two groups. Fig. 3 shows a scatter plot of the association of the change in PRU and the postprocedural PRU with the proximal reference lumen CSA. No statistically significant association was observed. The incidence rate of PMI was significantly higher in the greater than smaller increase group (59.1% vs. 34.8%, respectively; $p=0.008$) (Fig. 2B).

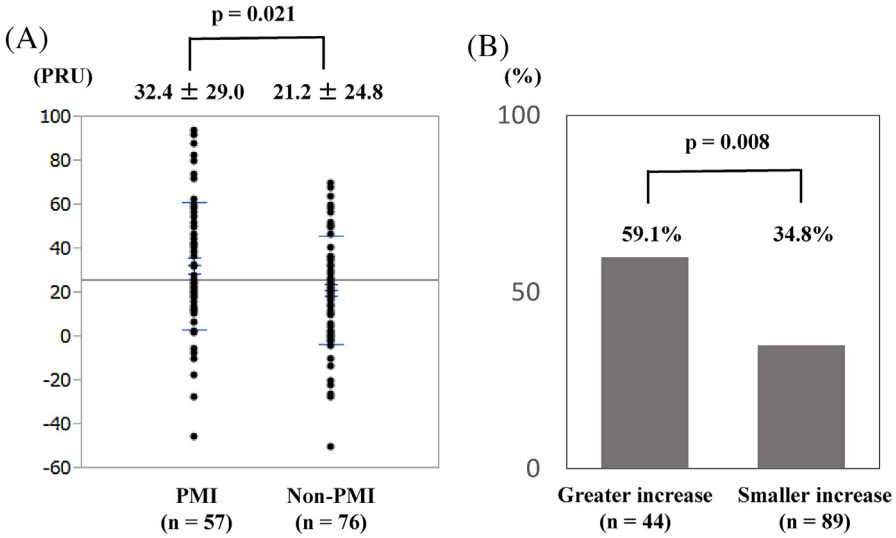

Fig. 2. (A) Absolute change of platelet reactivity during PCI in patients with or without PMI. (B) Incidence of PMI in greater (change in PRU of ≥37) and smaller (change in PRU of <37) increase groups. PCI, percutaneous coronary intervention; PMI, PCI-related myocardial infarction; PRU, P2Y12 reaction unit.

Table 3
Univariable and multivariable predictors of PMI.

	Univariable Odds ratio (95% CI)	*p*	Multivariable Odds ratio (95% CI)	*p*
Age, y	1.014 (0.980–1.050)	0.432	–	–
PRU value before PCI	0.998 (0.991–1.004)	0.486	–	–
Absolute change of PRU value	1.016 (1.002–1.030)	0.019	1.016 (1.002–1.031)	0.020
LDL-cholesterol, mg/dl	1.007 (0.995–1.019)	0.259	–	–
HDL-cholesterol, mg/dl	0.987 (0.957–1.016)	0.374	–	–
LDL/HDL ratio	1.461 (0.963–2.267)	0.075	1.423 (0.919–2.255)	0.115
Triglyceride, mg/dl	0.998 (0.994–1.002)	0.404	–	–
HbA1c, %	1.020 (0.743–1.393)	0.900	–	–
Creatinine, mg/dl	1.499 (0.383–5.932)	0.559	–	–
Mean stent diameter, mm	0.642 (0.307–1.310)	0.225	–	–
Total stent length, mm	1.023 (1.001–1.047)	0.038	1.021 (0.998–1.045)	0.071

PCI, percutaneous coronary intervention; PMI, PCI-related myocardial infarction; PRU, P2Y12 reaction unit; LDL, low-density lipoprotein; HDL, high-density lipoprotein; Hb, hemoglobin; CI, confidence interval.

Association between changes in platelet reactivity and thrombotic or hemorrhagic events 30 days after PCI

No thrombotic events had occurred by 30 days after PCI. A hemorrhagic event (BARC classification 3–5) occurred in only one woman in the greater increase group. She developed diverticular bleeding 12 days after PCI and received a blood transfusion because her hemoglobin level had decreased from 12.0 g/dl to 6.6 g/dl. Her platelet reactivity had increased from 199 PRU to 250 PRU during PCI.

Differences in plaque volume and remodeling index

A total of 71 patients underwent evaluation of imaging characteristics using IVUS. After exclusion of cases with poor image quality, the plaque volume and remodeling index could be evaluated in 41 patients. No significant differences were found between the PMI and non-PMI groups or between the greater and smaller increase groups. The results are shown in Supplement 2.

Discussion

The main findings of this study are as follows: platelet reactivity increased immediately after PCI; the absolute change in PRU was an independent predictor of PMI, and the optimal cut-off value was 37 PRU; and the proximal reference lumen area was significantly smaller in the greater increase group than in the smaller increase group. The incidence of peri-stent dissection was significantly higher in the greater increase group than in the smaller increase group.

Major studies have shown that high platelet reactivity in patients treated with clopidogrel is associated with an increased risk of PMI [9,10]. The optimal cut-off value for prediction of PMI was 240 PRU in these studies. In the present study, a very low proportion of patients (11.3%) had high platelet reactivity (defined as PRU of ≥240) before PCI, probably because of the use of prasugrel for antiplatelet therapy. However, the proportion of patients with high platelet reactivity was markedly increased after PCI (24.8%). Our results indicate that the increase in platelet reactivity during PCI might be associated with the incidence of PMI, even when platelet reactivity is substantially low before PCI. Previous studies have shown that arterial wall injury caused by PCI triggers transient hemostatic activation, leading to localized thrombosis and distal embolism. Strong and early activation of the hemostatic system occurs, which is possibly related to endothelial and atheromatous plaque disruption in response to balloon-induced arterial wall trauma [17,18]. Vascular endothelial damage during PCI leads to activation of platelet aggregation and subsequent distal embolism of microthrombi, and we considered that these distal embolisms are a major factor in the pathogenesis of PMI along with other lesion-related or procedural factors.

Table 4
Baseline, angiographic, procedural, and imaging characteristics of greater (change in PRU of ≥37) and smaller (change in PRU of <37) increase groups.

	Greater increase group ($n=44$)	Smaller increase group ($n=89$)	p
Absolute change of PRU value	55.5 ± 15.1	11.4 ± 18.6	<0.001
Age, y	71.8 ± 10.4	70.4 ± 10.1	0.443
Male	32 (72.7)	70 (78.7)	0.447
Coronary risk factor			
Hypertension	32 (72.7)	66 (74.2)	0.860
Dyslipidemia	30 (68.2)	65 (73.0)	0.560
Diabetes mellitus	25 (56.8)	47 (52.8)	0.662
Smoking	21 (47.7)	42 (47.2)	0.954
Chronic kidney disease	16 (36.4)	33 (37.1)	0.936
Preceding medication			
Calcium-channel blocker	15 (34.1)	37 (41.6)	0.405
β-Blocker	18 (40.9)	35 (39.3)	0.861
RAS-inhibitor	28 (63.6)	50 (56.2)	0.411
Statin	28 (63.6)	64 (71.9)	0.331
Insulin	6 (13.6)	8 (9.0)	0.411
DPP-4 inhibitor	11 (25.0)	30 (33.7)	0.306
Metformin	2 (4.6)	7 (7.9)	0.717
Laboratory data			
LDL-cholesterol, mg/dl	97.8 ± 29.2	99.4 ± 30.2	0.762
HDL-cholesterol, mg/dl	45.1 ± 10.1	47.2 ± 12.9	0.311
Triglyceride, mg/dl	141.3 ± 76.4	139.8 ± 89.0	0.920
HbA1c, %	6.6 ± 1.1	6.5 ± 1.1	0.605
Creatinine, mg/dl	0.9 ± 0.3	0.9 ± 0.2	0.912
eGFR, ml/m/1.73 m^2	64.2 ± 18.5	65.2 ± 16.9	0.760
Angiographic characteristics			
Left anterior descending artery	20 (45.5)	47 (52.8)	0.794
Left circumflex artery	8 (18.2)	17 (19.1)	0.898
Right coronary artery	18 (40.9)	28 (31.5)	0.281
Left main trunk	0 (0.0)	4 (4.5)	0.302
Multivessel disease	8 (18.2)	17 (19.1)	0.898
Type B2 or C	26 (59.1)	59 (66.3)	0.416
In-stent restenosis	4 (9.1)	5 (5.6)	0.478
QCA measurements			
Mean reference diameter, mm	2.2 ± 0.5	2.3 ± 0.6	0.644
Minimum lesion diameter, mm	0.7 ± 0.5	0.7 ± 0.4	0.568
Diameter stenosis, %	69.8 ± 15.9	67.6 ± 14.6	0.345
Lesion length, mm	18.5 ± 12.4	20.3 ± 14.1	0.537
Procedural characteristics			
Ad-hoc PCI	16 (36.4)	39 (43.8)	0.411
Procedural duration, min	82.4 ± 46.1	86.2 ± 37.0	0.648
Volume of contrast medium, ml	139.0 ± 46.8	137.9 ± 45.2	0.898
Total number of balloon dilatation	7.9 ± 4.5	9.1 ± 5.8	0.196
Max pressure of predilatation, atm	7.8 ± 2.4	9.5 ± 2.9	<0.001
Max pressure of postdilatation, atm	15.7 ± 4.3	16.3 ± 4.1	0.498
Mean stent diameter, mm	2.9 ± 0.5	2.9 ± 0.5	0.586
Total stent length, mm	28.0 ± 15.4	29.3 ± 17.3	0.641
Imaging characteristics			
Calcification (>180°)	15 (34.1)	29 (33.0)	0.896
Proximal reference EEM CSA, mm^2	13.8 ± 4.7	14.2 ± 4.4	0.754
Proximal reference lumen CSA, mm^2	6.5 ± 2.4	7.7 ± 3.1	0.032
Distal reference EEM CSA, mm^2	10.8 ± 4.5	10.4 ± 4.5	0.690
Distal reference lumen CSA, mm^2	5.6 ± 2.7	6.0 ± 3.0	0.507
Minimal stent area, mm^2	5.7 ± 2.1	6.0 ± 2.1	0.568
Incomplete stent apposition	4 (9.1)	12 (13.6)	0.451
Peri-stent dissection	10 (22.7)	6 (6.7)	0.008
Stent edge dissection	2 (4.6)	0 (0.0)	0.108

PMI is associated with patient-related factors, angiographic or lesion-related factors, and procedural factors [7]. Multi-vessel or diffuse coronary artery disease is a lesion-related factor associated with the occurrence of PMI [19,20]. A larger plaque volume and lipid-rich plaques are also indicative of embolic events after PCI resulting in myocardial injury [21]. Furthermore, the lipid profile is associated with the occurrence of PMI [22]. In the present study, the maximum post-dilatation pressure, mean stent diameter, and minimal stent area were similar between the two groups. However, the maximum pre-dilatation pressure was significantly lower in the greater than smaller increase group. The smaller vessel reference area in the greater increase group might have caused the lower pre-dilatation pressure to prevent excessive endothelial injury. In contrast, a greater difference in size between the lumen and stent may have led to peri-stent dissection more frequently in the greater increase group. It is possible that vascular endothelial damage caused by over-dilatation of stenting in small vessels might activate local platelet aggregation. Because platelet aggregability is directly related to systemic atherosclerotic disease [23], maintenance of sufficiently low platelet reactivity before PCI is recommended, especially in patients with multiple coronary risk factors and advanced atherosclerosis.

This study had some limitations. First, the sample size was relatively small. Because this was a pilot study, further analysis including a larger number of patients is needed to validate the association between the increase in platelet reactivity and PMI.

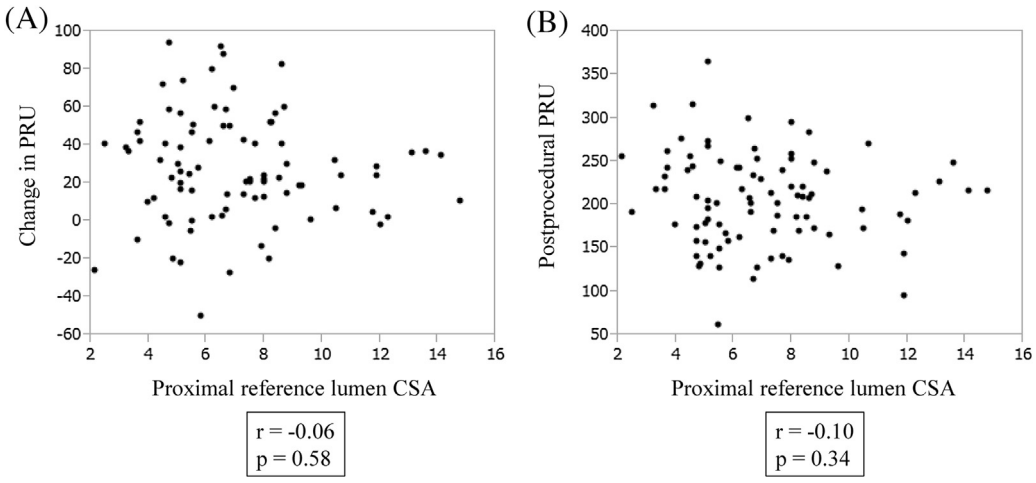

Fig. 3. Scatter plot of the association of (A) the change in the PRU value and (B) the postprocedural PRU value with the proximal reference lumen CSA. PRU, P2Y12 reaction unit; CSA, cross-sectional area.

Second, this study excluded patients with a high age, low body weight, and severely impaired liver and renal functions, which limits the applicability of these results to such patients.

Conclusion

Platelet reactivity is significantly increased after PCI and is involved in the incidence of PMI. The increase in platelet reactivity is associated with a small reference lumen area and occurrence of coronary dissection. Maintenance of substantially low platelet reactivity before PCI is important, especially in patients with a small reference lumen area in a culprit lesion. These findings should be validated in a larger study.

Conflicts of interest

HI received an honorarium from Daiichi Sankyo Co., Ltd. The other authors have no conflicts of interest in relation to the materials presented in this article.

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Appendix A. Supplementary data

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