

NEW RESEARCH PAPER

CORONARY

P2Y₁₂ Inhibitor Monotherapy Combined With Colchicine Following PCI in ACS Patients

The MACT Pilot Study



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ABSTRACT

BACKGROUND After a brief period of dual antiplatelet therapy, P2Y₁₂ inhibitor monotherapy in the absence of aspirin effectively reduces bleeding without increasing recurrent ischemia in patients undergoing percutaneous coronary intervention (PCI). In addition, early anti-inflammatory therapies may have clinical benefits in acute coronary syndrome (ACS) patients.

OBJECTIVES The aim of this study was to investigate the feasibility of ticagrelor or prasugrel P2Y₁₂ inhibitor monotherapy combined with colchicine immediately after PCI in patients with ACS.

METHODS This was a proof-of-concept pilot trial. ACS patients treated with drug-eluting stents were included. On the day after PCI, low-dose colchicine (0.6 mg daily) was administered in addition to ticagrelor or prasugrel maintenance therapy, whereas aspirin therapy was discontinued. The primary outcome was any stent thrombosis at 3 months. The key secondary outcomes were platelet reactivity measured by the VerifyNow assay (Accriva) before discharge and a reduction in high-sensitivity C-reactive protein (hs-CRP) over 1 month.

RESULTS We enrolled 200 patients, 190 (95.0%) of whom completed the 3-month follow-up. The primary outcome occurred in 2 patients (1.0%): 1 definite and 1 probable stent thrombosis. The level of platelet reactivity overall was 27 ± 42 P2Y₁₂ reaction units, and only 1 patient had high platelet reactivity (>208 P2Y₁₂ reaction units). The hs-CRP levels decreased from 6.1 mg/L (IQR: 2.6-15.9 mg/L) at 24 hours after PCI to 0.6 mg/L (IQR: 0.4-1.2 mg/L) at 1 month ($P < 0.001$), and the prevalence of high-inflammation criteria (hs-CRP ≥ 2 mg/L) decreased from 81.8% to 11.8% ($P < 0.001$).

CONCLUSIONS In ACS patients undergoing PCI, it is feasible to discontinue aspirin therapy and administer low-dose colchicine on the day after PCI in addition to ticagrelor or prasugrel P2Y₁₂ inhibitors. This approach is associated with favorable platelet function and inflammatory profiles. (Mono Antiplatelet and Colchicine Therapy [MACT];

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ABBREVIATIONS AND ACRONYMS

ACS = acute coronary syndrome

DAPT = dual antiplatelet therapy

DES = drug-eluting stent(s)

HPR = high platelet reactivity

hs-CRP = high-sensitivity C-reactive protein

LPR = low platelet reactivity

MI = myocardial infarction

PCI = percutaneous coronary intervention

PRU = P2Y₁₂ reaction unit

Dual antiplatelet therapy (DAPT) with aspirin and a P2Y₁₂ inhibitor has represented the standard of care for the prevention of thrombotic events in high-risk patients with coronary artery disease, such as patients with acute coronary syndrome (ACS) undergoing percutaneous coronary intervention (PCI).^{1,2} However, this strategy comes at the expense of increased bleeding, particularly when used long-term, underscoring the need to identify strategies associated with a more favorable safety profile without compromising efficacy.³ Studies have shown that the discontinuation of aspirin therapy after a brief period of DAPT (eg, 1-3 months) and main-

taining P2Y₁₂ inhibitor monotherapy reduces the risk of major bleeding without increasing the rate of ischemic events.⁴⁻⁹ However, more recent studies have shown that the risk of ischemic events may depend on the potency of the P2Y₁₂ inhibitor (ticagrelor or prasugrel vs clopidogrel), the clinical presentation (ACS vs stable ischemic heart disease), and the complexity of coronary artery disease or PCI.^{9,10}

In addition to antiplatelet therapy, anti-inflammatory agents may reduce recurrent ischemia in high-risk patients.¹¹⁻¹⁴ Among them, colchicine has been effective in a randomized clinical trial of patients with ACS.¹² The benefits of colchicine may be more beneficial with early (ie, in-hospital) initiation.¹⁵ These considerations support the rationale for testing a strategy that substitutes aspirin with colchicine during the acute phase to maximize the treatment effect of reducing recurrent ischemia and bleeding.

This study aimed to evaluate the feasibility of ticagrelor or prasugrel P2Y₁₂ inhibitor monotherapy in the absence of aspirin combined with colchicine in patients with ACS immediately after PCI.

METHODS

STUDY DESIGN. The MACT (Mono Antiplatelet and Colchicine Therapy) study was an investigator-initiated, single-center, single-arm, open-label, proof-of-concept pilot trial (NCT04949516). The

present study had a similar design to the ASET (Acetyl Salicylic Elimination Trial) (ie, a sample of 200 patients and a safety termination rule), which investigated the feasibility and safety of aspirin-free prasugrel maintenance immediately after PCI in patients with stable ischemic heart disease.¹⁶ There is no formal sample size rationale for the study because of the exploratory nature; however, if more than 3 cases of definite stent thrombosis occurred during the 3-month follow-up, patient recruitment was planned to be terminated.¹⁶ The study protocol was approved by the Institutional Review Board including the Ethics Committee of Wonkwang University Hospital.

STUDY POPULATION. Patients with non-ST-segment elevation ACS or ST-segment elevation myocardial infarction (MI) who underwent PCI with drug-eluting stents (DESs) were eligible ([Supplemental Methods](#)). Patients with the following conditions were excluded from the study: 1) cardiac arrest or cardiogenic shock; 2) age <19 or >90 years; 3) severe liver (Child-Pugh class C) or renal impairment (creatinine clearance <30 mL/min using the Cockcroft-Gault formula); 4) atrial fibrillation requiring anticoagulation therapy; 5) intolerance to prasugrel, ticagrelor, or colchicine; 6) history of intracranial hemorrhage; or 7) active bleeding. Written informed consent was obtained from all enrolled patients.

STUDY PROCEDURES. PCI with DES implantation was performed according to the standard of care. All patients received a loading dose of aspirin (300 mg) and ticagrelor (180 mg) or prasugrel (60 mg). The choice of ticagrelor or prasugrel was at the discretion of the treating physicians. The day after PCI, aspirin was discontinued, and colchicine (0.6 mg once daily) was administered with ticagrelor (90 mg twice daily) or prasugrel (10 mg once daily). In patients who received DES implantation with a loading dose of aspirin and clopidogrel, both were discontinued the day after PCI, with colchicine and a loading dose of ticagrelor or prasugrel started followed by maintenance doses. Staged PCI was performed under the maintenance of colchicine and ticagrelor or prasugrel. The concomitant use of other antiplatelet agents or anticoagulants was not permitted. However, readministration of aspirin was allowed for patient safety

The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the [Author Center](#).

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based on the results of platelet function testing (eg, cases of high platelet reactivity [HPR]) before discharge.

All patients underwent platelet function testing using the VerifyNow P2Y₁₂ assay (Accriva) before discharge, and levels of high-sensitivity C-reactive protein (hs-CRP) were measured at admission, 24 and 48 hours after PCI, and at the 1-month follow-up.

Clinical follow-up was performed at 1 and 3 months. Patient symptoms, treatment adherence, and clinical events were assessed using medical records. If an in-person visit was not possible, telephone interviews were performed. The Institutional Review Board monitored the study to identify potential adverse events that were not reported.

STUDY OUTCOMES. The primary outcome was stent thrombosis within 3 months of follow-up. Stent thrombosis was classified into definite, probable, or possible according to the Academic Research Consortium definition.¹⁷ The secondary outcomes were all-cause mortality; all MI; all revascularization; major bleeding¹⁸; a composite of cardiac death, target vessel MI, or target lesion revascularization; P2Y₁₂ reaction units (PRUs) using the VerifyNow P2Y₁₂ assay; and the change in hs-CRP levels between 24 hours after PCI and the 1-month follow-up. HPR (>208 PRUs) and low-platelet reactivity (LPR: <85 PRUs) were defined based on a prior consensus document,¹⁹ and elevated hs-CRP levels (≥ 2 mg/L) related to the risk of adverse cardiac events were defined based on prior studies.^{11,20} All clinical outcomes were independently adjudicated by the clinical event committee. The definition of clinical outcomes and the members of the clinical event committee are provided in the [Supplemental Methods](#).

In a post hoc analyses, the risk of bleeding and ischemia in the study population was assessed based on the PRECISE-DAPT (Predicting Bleeding Complications in Patients Undergoing Stent Implantation and Subsequent Dual Antiplatelet Therapy) score and the presence of complex PCI. The PRECISE-DAPT score of each patient was calculated using an online calculator. A PRECISE-DAPT score ≥ 25 was defined as high bleeding risk.²¹ Complex PCI was defined as having at least 1 of the following features: 3-vessel treatment, ≥ 3 stents implanted, ≥ 3 lesions treated, bifurcation with 2 stents implanted, total stent length >60 mm, and chronic total occlusion.¹⁰

STATISTICAL ANALYSIS. All analyses were performed based on the intention-to-treat principle. Continuous variables are reported as mean $\pm$ SD or median (IQR) and were compared using the *t*-test or Wilcoxon signed rank test. Categorical variables are

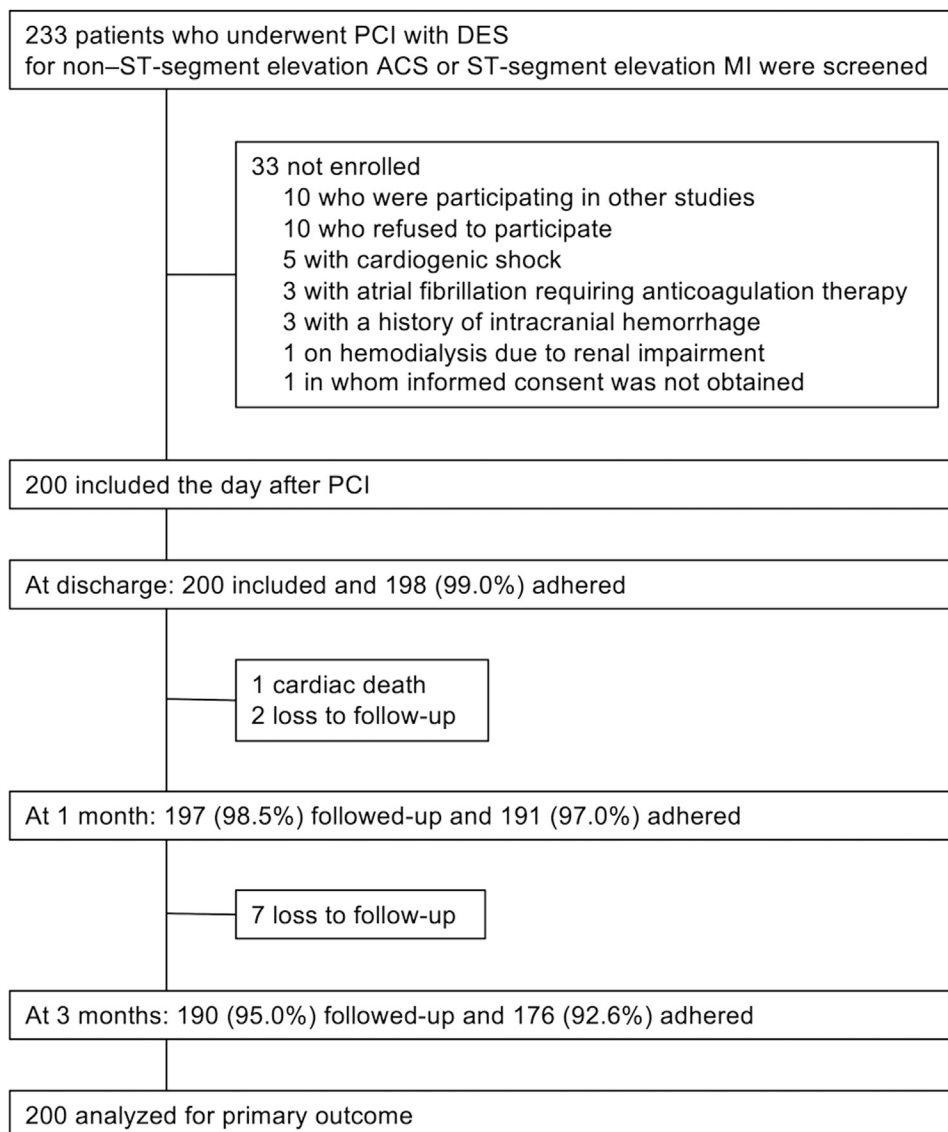
reported as numbers (percentages) and compared using the McNemar test. Kaplan-Meier estimates were used to determine the cumulative incidence of clinical events at 3 months. If a case was censored, the last available data were used for survival analysis. Statistical analyses were performed using SAS (version 9.2, SAS Institute). All tests were 2-sided, and statistical significance was set at $P < 0.05$.

RESULTS

PATIENT SCREENING AND ENROLLMENT. From June 2021 to September 2022, 233 patients with non-ST-segment elevation ACS or ST-segment elevation MI who underwent PCI with DESs were screened ([Figure 1](#)). Thirty-three patients were excluded for the following reasons: participation in another study ($n = 10$), patient refusal ($n = 10$), cardiogenic shock ($n = 5$), use of anticoagulation therapy ($n = 3$), prior intracranial hemorrhage ($n = 3$), hemodialysis ($n = 1$), and informed consent was not obtained ($n = 1$). Overall, 200 patients were included after the index PCI.

BASELINE CHARACTERISTICS. Clinical and angiographic characteristics of the patients are shown in [Table 1](#). The mean PRECISE-DAPT score was 14 ± 8 , and 11.5% of patients had a score ≥ 25 . Approximately 30% of the patients had multivessel disease, and the culprit lesion was detected in the left anterior descending artery in 54.5% of the patients. The procedural characteristics are shown in [Table 2](#). PCI through a radial access was performed in 60.9% of the patients, and sirolimus-eluting stents were used in 51.6% of the patients. After PCI, 95.3% of the treated lesions had Thrombolysis In Myocardial Infarction flow grade 3. Complex PCI was performed in 15.5% of the enrolled patients, and 9 patients (4.5%) underwent staged PCI. In addition, the baseline characteristics of patients with ST-segment elevation MI are reported in the [Supplemental Results](#).

ADHERENCE TO STUDY MEDICATIONS AND SERIOUS ADVERSE EVENTS. Adherence to study medications is shown in [Table 3](#). At discharge, 198 (99.0%) of the 200 patients followed the study procedure. At 1 month, 197 (98.5%) patients attended the clinical follow-up, and 191 (97.0%) followed the study procedure. At 3 months, 190 (95.0%) patients completed the clinical follow-up, and 176 (92.6%) followed the study procedure. Details regarding the adherence to study medications are described in the [Supplemental Results](#). Other than the study outcomes, no other procedure-related serious adverse events were reported.

FIGURE 1 Participant Flow

ACS = acute coronary syndrome; DES = drug-eluting stent(s); MI = myocardial infarction; PCI = percutaneous coronary intervention.

CLINICAL OUTCOMES. Clinical outcomes during the 3-month follow-up are shown in [Table 4](#). The primary outcome occurred in 2 patients (incidence 1.0%). The first case occurred 5 days after the index procedure in which a 2.75 × 38 mm amphilius-eluting stent (Cre8, CID SpA, member of Alvimedica) was implanted in the left anterior descending artery because of ST-segment elevation MI ([Supplemental Figure 1](#)). The patient received both aspirin and ticagrelor because of the HPR at discharge (242 PRUs). This definite subacute stent thrombosis was successfully

treated with balloon angioplasty ([Supplemental Figure 2](#)). After repeated PCIs, we were able to confirm that the patient was not compliant to antiplatelet medications. The platelet reactivity level decreased to 88 PRUs after supervised ticagrelor intake. The second case occurred 8 days after the index procedure in which a 2.75 × 30 mm sirolimus-eluting stent (Orsiro, Biotronik AG) was implanted in the left anterior descending artery because of ST-segment elevation MI ([Supplemental Figure 3](#)). The patient received ticagrelor and had LPR at discharge

(1 PRU). This probable subacute stent thrombosis was diagnosed based on the clinical criteria of an unexplained death. Neither patient underwent complex PCI.

Although bleeding occurred in 36 patients, major bleeding (Bleeding Academic Research Consortium type 3 or 5) occurred in only 1 patient (incidence 0.5%) with a PRECISE-DAPT score of 10. Gastrointestinal bleeding developed the day after PCI and was successfully treated with endoscopic hemostasis and transfusion. The patient was discharged with ticagrelor monotherapy (26 PRUs at discharge). No further clinical events occurred after discharge.

LABORATORY MEASUREMENTS. The level of platelet reactivity at discharge was 27 ± 42 PRUs (from the 191 analyzed patients). Most patients ($n = 174$, 91.1%) met the criteria for LPR, whereas only 1 patient (0.5%) met the criteria for HPR (Figure 2A). Platelet reactivity was similar in patients taking ticagrelor and prasugrel (29 ± 44 PRUs vs 26 ± 40 PRUs; $P = 0.65$) (Figure 2B). The level of inflammation was reduced considerably over time. After 1 month on study treatment, the hs-CRP level decreased from 6.1 mg/L (IQR: 2.6-15.9 mg/L) at 24 hours after PCI to 0.6 mg/L (IQR: 0.4-1.2 mg/L) ($P < 0.001$) (Figure 3A). Accordingly, the prevalence of high-inflammation criteria (hs-CRP ≥ 2 mg/L) decreased significantly (81.8% at 24 hours after PCI vs 11.8% at 1 month; $P < 0.001$) (Figure 3B). The data on platelet reactivity and inflammation in patients at high bleeding risk are reported in the Supplemental Results.

DISCUSSION

The present study is the first trial to evaluate the feasibility of P2Y₁₂ inhibitor monotherapy with ticagrelor or prasugrel in the absence of aspirin with colchicine therapy in patients with ACS immediately after PCI. The main findings of this study are as follows: 1) in ACS patients undergoing PCI, discontinuing aspirin therapy and administering low-dose colchicine (0.6 mg daily) on the day after PCI in addition to ticagrelor or prasugrel P2Y₁₂ inhibitors is associated with a low incidence of stent thrombosis (1.0%) at 3 months; 2) major bleeding is rare, with a 3-month incidence of 0.5%; 3) high platelet reactivity at discharge is low (0.5%); and 4) inflammatory levels were rapidly reduced within 1 month as shown by a significant decrease in hs-CRP levels. The low incidence of stent thrombosis reflects that reported by prior studies of patients undergoing PCI with DESs.²²

Over the last decade, a strategy of P2Y₁₂ inhibitor monotherapy after a brief period of DAPT has been

TABLE 1 Clinical and Angiographic Characteristics (N = 200)

Age, y	61.4 $\pm$ 10.7
Male	180 (90.0)
Height, cm	167.8 $\pm$ 6.2
Weight, kg	70.5 $\pm$ 10.2
Body mass index, kg/m ²	25.0 $\pm$ 3.1
Hypertension	103 (51.5)
Diabetes mellitus	61 (30.5)
Current smoking	96 (48.0)
Dyslipidemia	61 (30.5)
Previous myocardial infarction	12 (6.0)
Previous percutaneous coronary intervention	14 (7.0)
Previous coronary artery bypass grafting	1 (0.5)
Previous stroke	12 (6.0)
Clinical presentation	
Unstable angina	55 (27.5)
Non-ST-segment elevation myocardial infarction	52 (26.0)
ST-segment elevation myocardial infarction	93 (46.5)
Left ventricular ejection fraction on echocardiography, %	51.8 $\pm$ 8.5
<40%	14 (7.0)
PRECISE-DAPT score	14.4 $\pm$ 8.1
≥ 25	23 (11.5)
Medication use	
Statin	200 (100)
Beta-blocker	138 (69.0)
Angiotensin-converting enzyme inhibitor or angiotensin receptor blocker	136 (68.0)
Coronary artery disease	
1-vessel	143 (71.5)
2-vessel	39 (19.5)
3-vessel	18 (9.0)
Culprit lesion location	
Left main artery	2 (1.0)
Left anterior descending artery	109 (54.5)
Left circumflex artery	31 (15.5)
Right coronary artery	58 (29.0)

Values are mean $\pm$ SD or n (%).

PRECISE-DAPT = Predicting Bleeding Complications in Patients Undergoing Stent Implantation and Subsequent Dual Antiplatelet Therapy.

assessed in a number of randomized trials, including GLOBAL LEADERS (A Clinical Study Comparing Two Forms of Anti-platelet Therapy After Stent Implantation), STOPDAPT-2 (Short and Optimal Duration of Dual Antiplatelet Therapy-2 Study), STOPDAPT-2 ACS (Short and Optimal Duration of Dual Antiplatelet Therapy-2 Study for the Patients With ACS), SMART-CHOICE (Comparison Between P2Y₁₂ Antagonist Monotherapy and Dual Antiplatelet Therapy After DES), TWILIGHT (Ticagrelor with Aspirin or Alone in High-Risk Patients after Coronary Intervention), and TICO (Ticagrelor Monotherapy After 3 Months in the Patients Treated With New Generation Sirolimus-eluting Stent for Acute Coronary Syndrome).^{4-9,16} Among these, TICO and STOPDAPT-2 ACS were the

TABLE 2 Procedural Characteristics (N = 258)	
Preprocedural TIMI flow grade	
0	95 (36.8)
1	13 (5.0)
2	23 (8.9)
3	127 (49.2)
Radial access	157 (60.9)
Stent diameter, mm	3.1 ± 0.4
Stent length, mm	28.7 ± 12.0
Stent type	
Sirolimus-eluting stent	133 (51.6)
Everolimus-eluting stent	54 (20.9)
Amphilimus-eluting stent	52 (20.2)
Zotarolimus-eluting stent	14 (5.4)
Novolimus-eluting stent	5 (1.9)
Postdilatation with noncompliant balloon	100 (38.8)
Thrombus aspiration	7 (2.7)
Intravascular ultrasound use	16 (6.2)
Optical coherence tomography use	3 (1.2)
Postprocedural TIMI flow grade	
0	0
1	0
2	12 (4.7)
3	246 (95.3)
Number of patients	200
Number of vessels treated	1.2 ± 0.5
Number of lesions treated	1.3 ± 0.6
Number of stents implanted	1.4 ± 0.7
Total stent length, mm	36.9 ± 21.3
Complex percutaneous coronary intervention	31 (15.5)
3 vessels treated	5 (2.5)
≥3 lesions treated	7 (3.5)
≥3 stents implanted	15 (7.5)
Total stent length >60 mm	28 (14.0)
Bifurcation with 2 stents implanted	1 (0.5)
Chronic total occlusion	4 (2.0)
Values are n (%) or mean ± SD. TIMI = Thrombolysis in Myocardial Infarction.	

only trials specifically conducted in patients with ACS.^{8,9} The TICO study was the first randomized study to be conducted in patients with ACS. Its design was similar to that of the TWILIGHT study⁶; aspirin was discontinued 3 months after PCI, and the patients continued on ticagrelor maintenance therapy. The trial showed a significant reduction in the composite outcome of major bleeding and cardiovascular events at 1 year.⁸ However, the STOPDAPT-2 ACS study showed that aspirin discontinuation 1 to 2 months after PCI followed by clopidogrel maintenance therapy failed to achieve a net clinical benefit; additionally, there was an increase in cardiovascular events despite a reduction in bleeding.⁹ These contradictory findings suggest that aspirin has minimal additional

TABLE 3 Adherence to Study Medications (N = 200)	
P2Y ₁₂ inhibitors	200 (100)
Ticagrelor	104 (52.0)
Prasugrel	96 (48.0)
Clopidogrel	0
Colchicine	198 (99.0)
Aspirin	2 (1.0)
1-month follow-up	n = 197
P2Y ₁₂ inhibitors	194 (98.5)
Ticagrelor	99 (50.3)
Prasugrel	95 (48.2)
Clopidogrel	0
Colchicine	193 (98.0)
Aspirin	2 (1.0)
3-month follow-up	n = 190
P2Y ₁₂ inhibitors	182 (95.8)
Ticagrelor	91 (47.9)
Prasugrel	89 (46.8)
Clopidogrel	2 (1.1)
Colchicine	183 (96.3)
Aspirin	5 (2.6)
Values are n (%).	

efficacy in the presence of effective P2Y₁₂ inhibition. A potent P2Y₁₂ inhibitor alone inhibits platelet aggregation, which is marginally enhanced by aspirin.^{23,24} Potent P2Y₁₂ inhibitors reportedly down-regulate other markers of platelet reactivity, including arachidonic acid- and collagen-induced aggregation.^{25,26} Nevertheless, aspirin is still recommended immediately after PCI for its additive effect of preventing thrombosis that may be partly induced by stenting injury and subsequent subendothelial collagen exposure.^{2,27} Moreover, thrombogenicity is enhanced with myocardial injury during the acute to subacute phase in ACS patients, making post-PCI DAPT a necessity. However, the immediate aspirin withdrawal after PCI has been extensively studied in patients with concomitant use of oral anti-coagulation.²⁸ In this setting, it has been highlighted as the best strategy.

In addition to the ASET study,¹⁶ the OPTICA (Optimised Computed Tomography Pulmonary Angiography in Pregnancy, Quality and Safety Study) recently showed that ticagrelor or prasugrel mono antiplatelet therapy directly after PCI was feasible in patients with non-ST-segment elevation ACS.²⁹ The present results extend its possibility into all ACS patients including ST-segment elevation MI. In our study, aspirin was discontinued without checking platelet reactivity to consider its potential application in clinical practice because platelet

TABLE 4 Clinical Outcomes at 3 Months

Definite, probable, or possible stent thrombosis	2 (1.0)
Definite stent thrombosis	1
Probable stent thrombosis	1
Possible stent thrombosis	0
All-cause death	1 (0.5)
Cardiac death	1
All MI	1 (0.5)
Target vessel MI	1
All revascularization	2 (1.0)
Target lesion revascularization	1
All-cause death, all MI, or all revascularization	3 (1.5)
Cardiac death, target vessel MI, or target lesion revascularization	2 (1.0)
All bleeding	36 (18.0)
BARC type 1	15
BARC type 2	20
BARC type 3	1
BARC type 5	0
BARC type 2, 3, or 5	21 (10.5)
BARC type 3 or 5	1 (0.5)

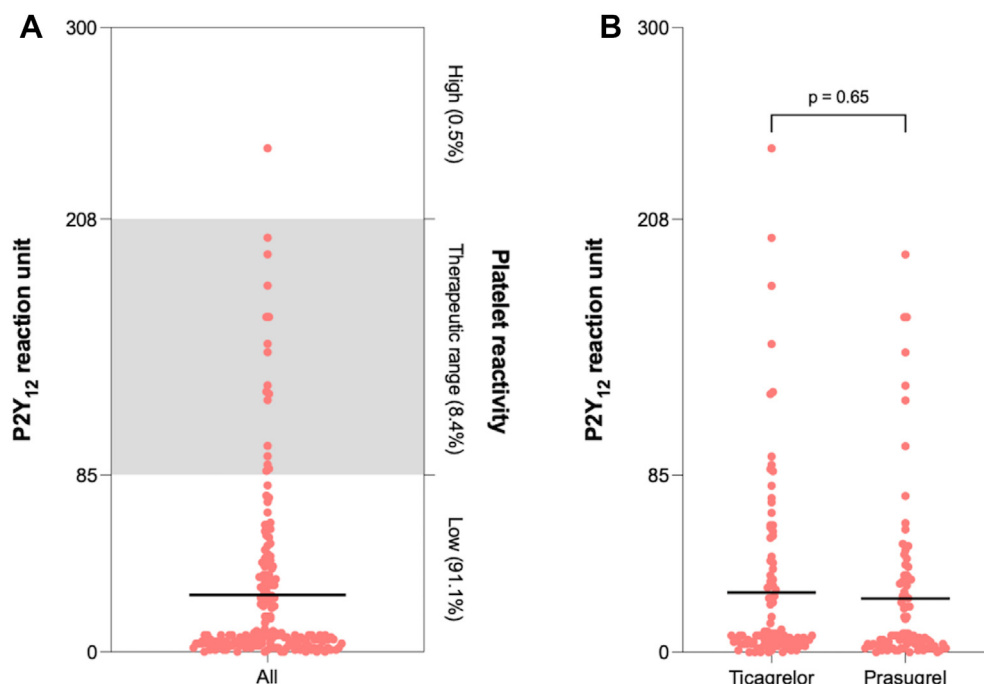
Values are n or n (Kaplan-Meier estimates).

BARC = Bleeding Academic Research Consortium; MI = myocardial infarction.

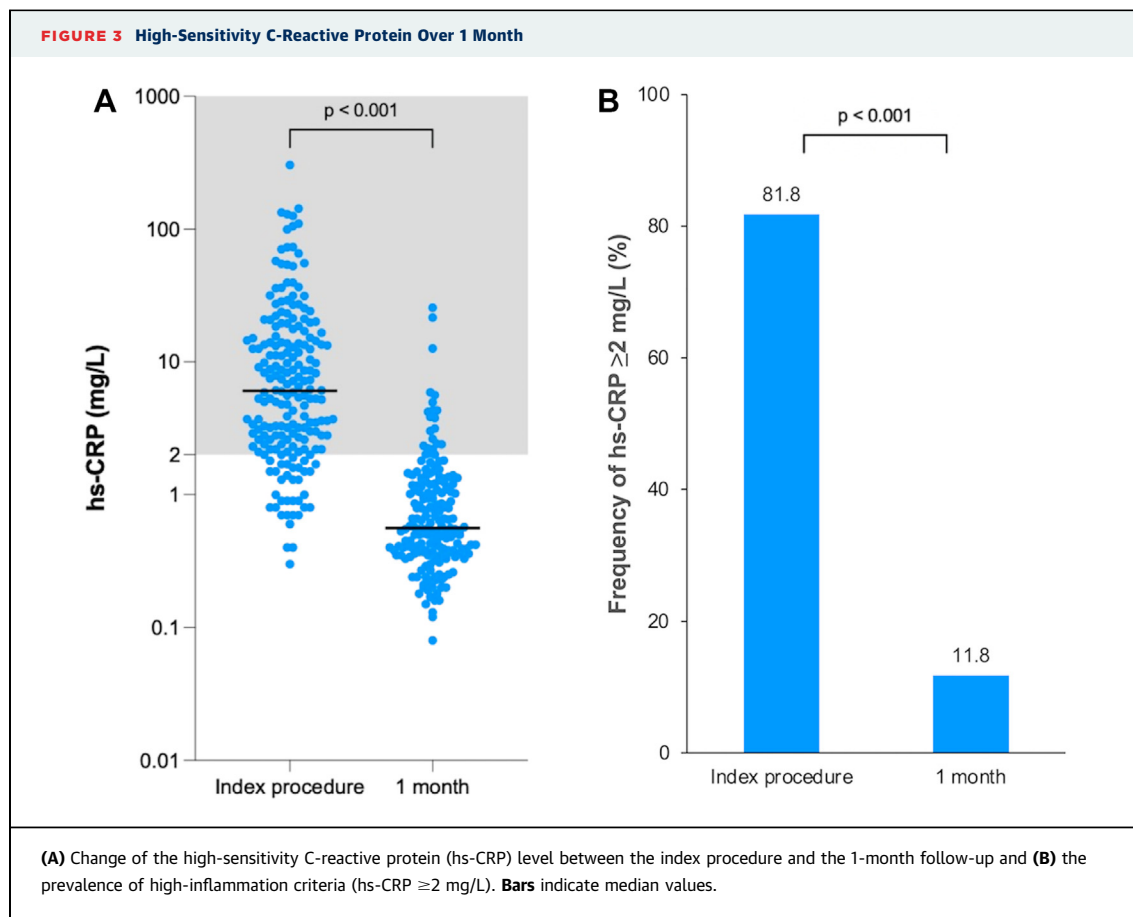
function testing is not routinely recommended after PCI.^{1,2} Most patients had LPR at discharge, and definite stent thrombosis occurred only in the patient with HPR. Therefore, potent inhibition of the P2Y₁₂ signaling pathway by ticagrelor or prasugrel may enable immediate aspirin discontinuation because of its limited additional antiplatelet effects. The present results suggest that the potential benefits of the immediate discontinuation of aspirin are primarily caused by the reduction in major bleeding, which frequently occurs before discharge or within 1 month after PCI. In the TICO substudy, half of the major bleeds occurred within 1 month of DES implantation.³⁰ About 90% of the enrolled patients showed excessive platelet inhibition (<85 PRUs), and direct discontinuation of aspirin may have potential to reduce the risk of major bleeding.

Inflammation plays a fundamental role in the development and progression of the atherothrombotic process.³¹ Thus, anti-inflammatory agents are beneficial in a range of cardiovascular conditions. Leukocytes uptake colchicine. Its ability to bind to tubulin and interfere with microtubular function affects the expression of cytokines and interleukins and

FIGURE 2 Platelet Reactivity Before Discharge



(A) Distribution of platelet reactivity measured by the VerifyNow test before discharge and (B) platelet reactivity on ticagrelor versus prasugrel therapy. Bars indicate mean values.



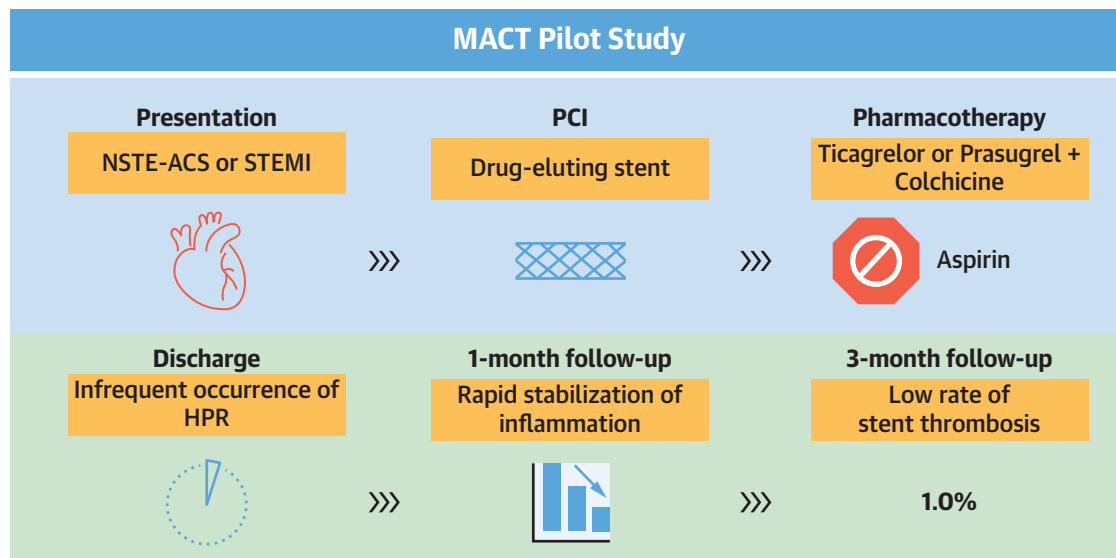
the ability of neutrophils to marginate, ingress, aggregate, express superoxide, release neutrophil extracellular traps, and interact with platelets.³² Colchicine’s efficacy has been well established by the COLCOT (Colchicine Cardiovascular Outcomes Trial) and LoDoCo2 (Low Dose Colchicine for Secondary Prevention of Cardiovascular Disease 2) randomized clinical trials in which low-dose colchicine significantly reduced the risk of ischemic cardiovascular events.^{12,13} In a subanalysis of the COLCOT study, there was a significant reduction in the incidence of ischemic events in patients in whom colchicine was initiated within 3 days of the index MI.¹⁵ In addition, colchicine has been shown to exert antiplatelet effects in vitro via the inhibition of key proteins involved in cytoskeleton rearrangement.³³ However, clinical data regarding the early administration of colchicine in patients with ACS who have been treated with PCI are limited.³⁴

In the present study, inflammatory levels were rapidly reduced. In the acute phase of MI, cardiomyocyte necrosis generates damage-associated molecular patterns, which in turn activate the

complement cascade and stimulate toll-like receptor and interleukin-1 signaling.^{35,36} These factors trigger an intense inflammatory response that may lead to adverse myocardial remodeling.³⁷ Furthermore, MI liberates hematopoietic stem and progenitor cells from the bone marrow niches via the sympathetic nervous system, which accelerates systemic atherosclerosis by recruiting monocytes within the plaques.³⁸ Because colchicine is preferentially concentrated in leukocytes, its anti-inflammatory effects are marked at low doses.³² Moreover, colchicine may prevent MI-related Dressler syndrome, which was not observed in the present study. Similar to other studies,^{12,13} low-dose colchicine was tolerable for immediate administration after PCI and subsequent maintenance dosing.

In addition to the prespecified analyses, we evaluated the bleeding and ischemic risks of patients according to the PRECISE-DAPT score and PCI complexity. Most patients in the present study were at low risk of bleeding and did not undergo complex PCI. A substudy of the SMART-DATE (6- Versus 12-Month or Longer Dual Antiplatelet Therapy After

CENTRAL ILLUSTRATION The Overview of Mono Antiplatelet and Colchicine Therapy



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Ticagrelor or Prasugrel Mono Antiplatelet and Colchicine Therapy Is Feasible Immediately After PCI in ACS. HPR = high platelet reactivity; MACT = Mono Antiplatelet and Colchicine Therapy; NSTE-ACS = non-ST-segment elevation acute coronary syndrome; PCI = percutaneous coronary intervention; STEMI = ST-segment elevation myocardial infarction.

Percutaneous Coronary Intervention in Patients With Acute Coronary Syndrome) trial indicated that the prevalence of ACS in patients at high bleeding risk was 27.5%.³⁹ Giustino et al¹⁰ defined complex PCI and determined that its frequency was 17.5% in a pooled data set that included 6 randomized clinical trials. The present study mostly included ACS patients with hemodynamic stability; our cohort may under-represent patients with bleeding or ischemic risk met in daily practice. Nevertheless, the advantage of immediate aspirin withdrawal might be particularly attractive in patients at high bleeding risk with an impact on relevant endpoints.⁴⁰ Therefore, further studies are warranted to evaluate the efficacy and safety of this experimental strategy, especially in patients at high bleeding or ischemic risk.

STUDY LIMITATIONS. First, all enrolled patients were Asian who were at relatively low bleeding and ischemic risk. Although ticagrelor or prasugrel is effective regardless of ethnicity,⁴¹ clinical data supporting this de-escalation strategy are limited.

Second, there was no control group for comparison with the experimental group. Thus, it is not clear whether the reduction of hs-CRP resulted from colchicine or the physiologic response after ACS. Third, this study did not evaluate long-term clinical outcomes, and there was a relatively high rate of patients who were lost to follow-up despite the relatively brief duration of follow-up. Fourth, compliance with study medications was only assessed as reported by the patient and may therefore not have reflected true compliance. Lastly, the association between hs-CRP on admission and platelet reactivity was not evaluated.⁴²

CONCLUSIONS

The feasibility of discontinuing aspirin therapy and administering low-dose colchicine on the day after PCI in addition to ticagrelor or prasugrel P2Y₁₂ inhibitors with associated benefits for platelet function and inflammatory profiles in ACS patients warrants further investigation (**Central Illustration**).

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PERSPECTIVES

WHAT IS KNOWN? Aspirin-free P2Y₁₂ inhibitor monotherapy combined with specific anti-inflammatory therapy may maximize the treatment effect of reducing both bleeding and ischemia, especially in ACS patients undergoing PCI.

WHAT IS NEW? In ACS patients undergoing PCI, it is feasible to discontinue aspirin therapy and administer low-dose colchicine (0.6 mg daily) on the day after PCI in addition to ticagrelor or prasugrel P2Y₁₂ inhibitors. This finding is associated with the marked inhibition of platelet reactivity and the rapid stabilization of inflammation after ACS.

WHAT IS NEXT? Further studies are required to compare this explorative strategy with standard treatment in terms of platelet reactivity, post-ACS inflammatory response, and clinical outcome.

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KEY WORDS acute coronary syndrome, aspirin, colchicine, prasugrel, ticagrelor

APPENDIX For expanded Methods and Results sections and supplemental figures, please see the online version of this paper.