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ORIGINAL RESEARCH

Optimal timing of aspirin discontinuation with ticagrelor monotherapy in acute coronary syndrome: a *post hoc* comparative analysis from the TICO and T-PASS trials

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ABSTRACT

BACKGROUND: Ticagrelor monotherapy following abbreviated dual antiplatelet therapy (DAPT) is an emerging strategy for patients with acute coronary syndrome (ACS) undergoing percutaneous coronary intervention (PCI). However, the timing of aspirin discontinuation has not been directly compared in this setting.

AIMS: We aimed to compare the clinical outcomes of aspirin discontinuation within 1 month versus at 3 months after PCI in patients with ACS.

METHODS: This *post hoc* analysis used individual patient-level data from the TICO and T-PASS trials, which exclusively enrolled patients with ACS undergoing PCI. Of 2,953 patients who received ticagrelor monotherapy after abbreviated DAPT, 1,426 discontinued aspirin within 1 month and 1,527 at 3 months. After propensity score matching, 2,248 patients were included in the final analysis. The primary endpoint was a composite of all-cause death, myocardial infarction, stent thrombosis, ischaemia-driven target vessel revascularisation, stroke, and major bleeding at 1 year.

RESULTS: The primary endpoint occurred less frequently in the <1-month group than in the 3-month group (3.2% vs 5.6%; hazard ratio [HR] 0.56, 95% confidence interval [CI]: 0.37-0.84; p=0.005). Ischaemic event rates were comparable (2.2% vs 2.3%; HR 0.86, 95% CI: 0.55-1.65; p=0.863), whereas major bleeding was significantly lower in the <1-month group (1.1% vs 3.3%; HR 0.32, 95% CI: 0.17-0.61; p<0.001). Landmark analysis showed that event rates diverged primarily within the first 90 days, with no significant heterogeneity between the early and late periods.

CONCLUSIONS: Aspirin discontinuation within 1 month followed by ticagrelor monotherapy improved net clinical outcomes compared with 3-month discontinuation, primarily by reducing major bleeding without increasing ischaemic risk. ClinicalTrials.gov: NCT02494895 (TICO), NCT03797651 (T-PASS).

KEYWORDS: acute coronary syndrome; aspirin; dual antiplatelet therapy; percutaneous coronary intervention; ticagrelor

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Dual antiplatelet therapy (DAPT), a combination of aspirin and $P2Y_{12}$ inhibitors, is essential for managing patients with acute coronary syndrome (ACS) who have undergone percutaneous coronary intervention (PCI). Compared with clopidogrel-based DAPT, a more potent $P2Y_{12}$ inhibitor, such as prasugrel or ticagrelor, provides stronger and more consistent platelet inhibition, resulting in improved clinical outcomes in these patients[1,2]. Current ACS guidelines recommend a potent $P2Y_{12}$ inhibitor over clopidogrel for at least 12 months following PCI with drug-eluting stents (DES)[3,4]. However, these strategies may be accompanied by an increased risk of bleeding, a complication associated with poor clinical outcomes[5,6].

To optimise the balance between ischaemic and bleeding risks, several randomised clinical trials have evaluated the efficacy and safety of an aspirin-discontinuation strategy followed by ticagrelor monotherapy[7-10]. Among these, the Ticagrelor Monotherapy After 3 Months in the Patients Treated With New Generation Sirolimus Stent for Acute Coronary Syndrome (TICO) and Ticagrelor Monotherapy in PAtients Treated With New-generation Drug-eluting Stents for Acute Coronary Syndrome (T-PASS) trials exclusively enrolled patients with ACS treated with DES and demonstrated the efficacy and safety of ticagrelor monotherapy following abbreviated DAPT[9,10]. In accordance with these findings, the most recent American guidelines provide a Class I recommendation for ticagrelor monotherapy after 1-3 months of DAPT in patients with ACS to reduce bleeding risk[11]. However, the optimal timing of aspirin discontinuation, specifically within 1 month versus at 3 months, has not been evaluated in these patients. Therefore, we aimed to compare the clinical efficacy and safety of aspirin discontinuation within 1 month versus at 3 months after PCI with subsequent ticagrelor monotherapy in patients with ACS, using individual patient data from the TICO and T-PASS trials.

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Impact on daily practice

In patients with acute coronary syndrome undergoing percutaneous coronary intervention, aspirin discontinuation within 1 month followed by ticagrelor monotherapy was associated with fewer net clinical adverse events compared with 3-month discontinuation. This benefit was primarily driven by a significant reduction in major bleeding without an increase in ischaemic complications. These findings add to the growing evidence supporting abbreviated ticagrelor-based dual antiplatelet therapy strategies to optimise the balance between ischaemic and bleeding risks.

Methods

STUDY POPULATION AND PROCEDURES

We performed a *post hoc* comparative analysis using merged datasets from the TICO and T-PASS trials. Although both trials were randomised, the present analysis was observational in nature and excluded patients assigned to the conventional 12-month DAPT regimen. After merging the datasets and excluding patients on the 12-month DAPT regimen, a total of 2,953 patients with ACS who received ticagrelor monotherapy after abbreviated DAPT were identified. The <1-month group (n=1,426) was derived from the T-PASS trial, whereas the 3-month group (n=1,527) was derived from the TICO trial. **Figure 1** illustrates the selection process for the study population.

The TICO trial, an investigator-initiated, multicentre, randomised, unblinded trial conducted at 38 centres in the Republic of Korea, enrolled 3,056 patients who underwent PCI for ACS[9]. After successful PCI, patients were randomised in a 1:1 ratio to conventional ticagrelor-based 12-month DAPT or aspirin discontinuation at 3 months followed by ticagrelor monotherapy[9]. A total of 1,527 patients were assigned to the 3-month aspirin discontinuation group between August 2015 and October 2018, with 1,339 patients (88%) compliant with the assigned treatment. Similarly, the T-PASS trial was conducted at 24 centres in the Republic of Korea and included a total of 2,850 patients with ACS[10]. In this trial, patients were randomised in a 1:1 ratio to ticagrelor-based 12-month DAPT or aspirin discontinuation within 1 month after DES implantation between April 2019 and May 2022. A total of 1,426 patients were assigned to the <1-month group, and discontinuation occurred after a median of 16 days (interquartile range [IQR] 12-25 days). Of these, 1,221 patients (86%) adhered to the assigned treatment protocol, with no significant differences in the adherence rates between the groups. The reasons for non-compliance have been detailed in previous reports[9,10]. The detailed inclusion and exclusion criteria of the two trials are summarised in **Supplementary Table 1**.

In both trials, PCI was performed using bioresorbable polymer sirolimus-eluting stents (Orsiro [Biotronik]) and standard techniques. At the time of index PCI, loading doses of aspirin (300 mg) and ticagrelor (180 mg) were administered if the patient was not already taking these drugs. Thereafter, ticagrelor was prescribed at a maintenance dose of 90 mg twice daily according to the study protocol. The study population was not permitted to use concomitant antiplatelet agents or anticoagulants. Other cardiovascular medications, such as lipid-lowering or antihypertensive therapies, were administered according to current guidelines.

STUDY ENDPOINTS AND DEFINITIONS

The primary endpoint was net adverse clinical events, defined as a composite of all-cause mortality, myocardial infarction, stent thrombosis, ischaemia-driven target vessel revascularisation, stroke, and major bleeding within 1 year. Post-discharge myocardial infarction was identified by ischaemic symptoms, electrocardiographic changes, or imaging findings combined with elevated cardiac biomarkers exceeding the 99th percentile of the upper reference limit[12].

Abbreviations

ACS	acute coronary syndrome	**DAPT**	dual antiplatelet therapy	**PCI**	percutaneous coronary intervention
BARC	Bleeding Academic Research Consortium	**DES**	drug-eluting stent		

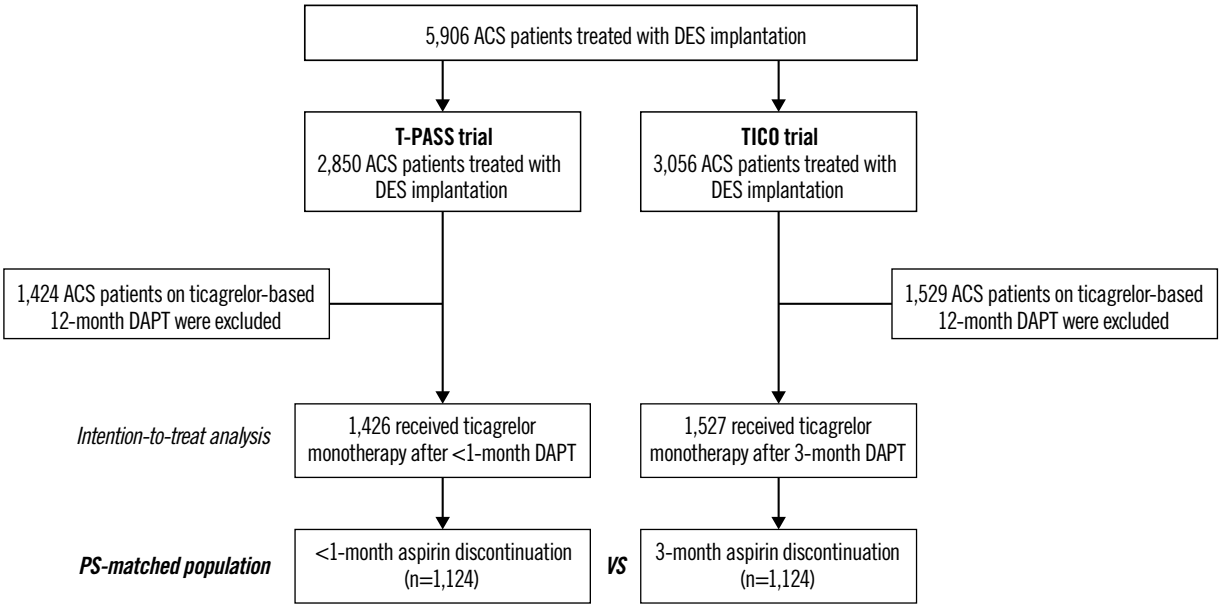


Figure 1. *The selection process of the study population. ACS: acute coronary syndrome; DAPT: dual antiplatelet therapy; DES: drug-eluting stent; PS: propensity score; T-PASS: Ticagrelor Monotherapy in PAtients Treated With New-generation Drug-eluting Stents for Acute Coronary Syndrome; TICO: Ticagrelor Monotherapy After 3 Months in the Patients Treated With New Generation Sirolimus Stent for Acute Coronary Syndrome*

Stent thrombosis was defined as definite or probable events based on the Academic Research Consortium definitions[13]. Ischaemia-driven target vessel revascularisation was defined as repeat PCI or coronary artery bypass grafting for a target vessel with >50% stenosis and evidence of myocardial ischaemia, including clinical symptoms or a positive stress test[14]. Stroke was characterised as the presence of acute neurological symptoms confirmed by brain imaging[14]. Major bleeding events were defined as Bleeding Academic Research Consortium Type 3 or 5 bleeding[15].

Secondary endpoints included the individual components of the primary endpoint as well as major adverse cardiac and cerebrovascular events, which were defined as a composite of all-cause death, myocardial infarction, stent thrombosis, ischaemia-driven target vessel revascularisation, and stroke.

STATISTICAL ANALYSIS

The intention-to-treat principle was implemented based on the initial randomisation groups to analyse individual patient data. Categorical variables are presented as n (%) and were compared using the chi-square or Fisher's exact test. Continuous variables are expressed as mean±standard deviation or median (IQR) and were analysed using Student's t-test or the Mann-Whitney U test, depending on the distribution of the data.

Propensity score matching was used to construct a balanced 1:1 matched cohort between the <1-month and 3-month groups. Propensity scores were calculated using multivariable logistic regression analysis incorporating baseline clinical, lesion, and procedural variables. Patients were matched using nearest-neighbour matching without replacement and a calliper width of 0.03. Standardised mean differences <10% were used to confirm balance across covariates after matching. Model calibration and discrimination were assessed using the Hosmer-Lemeshow test and Harrell's C-index[16].

In the propensity score-matched population, Kaplan-Meier survival curves were constructed to estimate event rates, and differences in event-free survival were compared using the log-rank test. A prespecified 3-month landmark analysis was conducted because antiplatelet regimens differed between the groups during the first 3 months (aspirin discontinuation within 1 month vs continued ticagrelor-based DAPT) and became identical thereafter (ticagrelor monotherapy). Cox proportional hazards regression analysis was used to identify independent predictors of the primary endpoint in the propensity score-matched population, and hazard ratios (HRs) with 95% confidence intervals (CIs) are reported. Variables with p-values<0.10 in the univariate analysis were included in the multivariable model. Subgroup analyses were performed based on prespecified factors, including age, sex, diabetes mellitus, hypertension, chronic kidney disease, clinical presentation, presence of multivessel disease, total stent length, and vascular access. Adjusted HRs were calculated using multivariable Cox regression analysis, incorporating clinical and procedural variables.

All statistical analyses were performed using SPSS, version 26.0 (IBM) and R, version 4.2.2 (R Foundation for Statistical Computing). Statistical significance was set at p<0.05.

Results

The baseline clinical, angiographic, and procedural characteristics of the overall population are shown in **Supplementary Table 2**. After propensity score matching, 1,124 patients were included in each group, and the groups were well balanced across clinical, lesion, and procedural variables **(Table 1)**. In the propensity score-matched

Table 1. Clinical, angiographic, and procedural characteristics in the propensity score-matched population.

	<1-month aspirin discontinuation[a] (n=1,124)	3-month aspirin discontinuation (n=1,124)	*p*-value
Age, years	60.4±10.6	60.4±10.8	0.939
Male	919 (81.8)	901 (80.2)	0.334
Body mass index, kg/m^2	25.0±3.4	24.9±3.2	0.654
Hypertension	544 (48.4)	549 (48.8)	0.833
Diabetes mellitus	309 (27.5)	305 (27.1)	0.850
Diabetes mellitus with insulin	31 (2.8)	32 (2.8)	0.898
Chronic kidney disease[b]	112 (10.0)	141 (12.5)	0.053
End-stage kidney disease on dialysis	6 (0.5)	10 (0.9)	0.316
Dyslipidaemia	768 (68.3)	751 (66.8)	0.444
Current smoker	428 (38.1)	434 (38.6)	0.795
Prior myocardial infarction	27 (2.4)	28 (2.5)	0.891
Prior percutaneous coronary intervention	83 (7.4)	93 (8.3)	0.432
Prior coronary artery bypass graft surgery	3 (0.3)	5 (0.4)	0.479
Prior stroke	39 (3.5)	40 (3.6)	0.909
Clinical presentation			0.661
Unstable angina	295 (26.2)	277 (24.6)	
Non-ST-segment elevation MI	397 (35.3)	411 (36.6)	
ST-segment elevation MI	432 (38.4)	436 (38.8)	
Transradial approach	698 (62.1)	673 (59.9)	0.280
Use of IABP	13 (1.2)	14 (1.2)	0.846
Use of ECMO	3 (0.3)	4 (0.4)	0.705
Multivessel disease	602 (53.6)	622 (55.3)	0.397
Left main disease	23 (2.0)	22 (2.0)	0.880
Bifurcation disease	174 (15.5)	169 (15.0)	0.769
Use of glycoprotein IIb/IIIa inhibitors	72 (6.4)	83 (7.4)	0.360
Use of thrombectomy	59 (5.2)	53 (4.7)	0.561
Multilesion intervention	232 (20.6)	221 (19.7)	0.563
Multivessel intervention	185 (16.5)	179 (15.9)	0.731
Treated lesions per patient	1.0 [1.0-1.0]	1.0 [1.0-1.0]	0.595
Total number of stents per patient	1.0 [1.0-2.0]	1.0 [1.0-2.0]	0.724
Total stent length per patient, mm	30.0 [22.0-41.0]	26 [22.0-40.0]	0.099

Data are reported as N (%), mean±standard deviation, or median [IQR]. [a]Aspirin was discontinued after a median of 16 days [IQR 12-25] in the <1-month group. [b]Chronic kidney disease was defined as an estimated glomerular filtration rate of less than 60 mL/min/1.73 m^2 of body surface area.
ECMO: extracorporeal membrane oxygenation; IABP: intra-aortic balloon pump; IQR: interquartile range; MI: myocardial infarction

population, aspirin was discontinued at a median of 16 days (IQR 12-25) after PCI in the <1-month group. The mean age of the cohort was 60.4 years, and approximately 81.0% of patients were male. Overall, across both groups, the prevalence of hypertension and diabetes mellitus were 48.6% and 27.3%, respectively, and ST-segment elevation myocardial infarction accounted for 38.6% of the clinical presentations.

The 1-year clinical outcomes of the propensity score-matched population are summarised in **Table 2**. The median follow-up duration was 365 days for both groups. The primary endpoint occurred less frequently in the <1-month group than in the 3-month group (3.2% vs 5.6%; HR 0.56, 95% CI: 0.37-0.84; p=0.005) **(Figure 2A)**. The incidence of major adverse cardiac and cerebrovascular events was similar between the two groups (2.2% vs 2.3%; HR 0.86, 95% CI: 0.55-1.65; p=0.863) **(Figure 2B)**, whereas the rate of major bleeding was significantly lower in the <1-month group than in the 3-month group over 12 months (1.1% vs 3.3%; HR 0.32, 95% CI: 0.17-0.61; p<0.001) **(Figure 2C)**. When comparing the groups in the 3-month landmark analysis, the primary event rates diverged within the first 90 days (HR 0.55, 95% CI: 0.32-0.94; p=0.013) **(Figure 2D)**. However, the interaction p-value (p=0.79) indicated no significant heterogeneity in the treatment effect between the early and late periods. When assessing the overall unmatched population, the results were

Table 2. Clinical outcomes at 1 year in the propensity score-matched population.

	<1-month aspirin discontinuation (n=1,124)	3-month aspirin discontinuation (n=1,124)	HR (95% CI)	*p*-value
Primary endpoint				
Net adverse clinical events[a]	36 (3.2)	63 (5.6)	0.56 (0.37-0.84)	0.005
Secondary endpoints				
Major adverse cardiac and cerebrovascular events[b]	25 (2.2)	26 (2.3)	0.86 (0.55-1.65)	0.863
Major bleeding[c]	12 (1.1)	37 (3.3)	0.32 (0.17-0.61)	<0.001
BARC Type 3	12 (1.1)	37 (3.3)	0.32 (0.17-0.61)	<0.001
BARC Type 5	0 (0)	0 (0)	-	–
Cardiac death, myocardial infarction, or stroke	13 (1.2)	17 (1.5)	0.84 (0.50-1.41)	0.453
All-cause death	8 (0.7)	12 (1.1)	1.00 (0.48-2.10)	0.361
Cardiac death	1 (0.1)	6 (0.5)	0.67 (0.24-1.88)	0.058
Myocardial infarction	6 (0.5)	4 (0.4)	0.88 (0.32-2.41)	0.534
Stent thrombosis	2 (0.2)	4 (0.4)	1.00 (0.14-7.09)	0.412
Subacute	2	4	-	
Late	0	0	-	
Stroke	6 (0.5)	7 (0.6)	0.73 (0.29-1.81)	0.768
Ischaemic	6	5	-	
Haemorrhagic	0	2	-	
Ischaemia-driven target vessel revascularisation	8 (0.7)	4 (0.4)	0.61 (0.29-1.29)	0.256

Data are presented for the intention-to-treat population and the number of patients with event(s) (% are Kaplan-Meier estimates at day 360). [a]Net adverse clinical events included the composite of major adverse cardiac and cerebrovascular events and major bleeding. [b]Major adverse cardiac and cerebrovascular events included the composite of all-cause death, myocardial infarction, stent thrombosis, ischaemia-driven target vessel revascularisation, and stroke. [c]Major bleeding included the composite of BARC Types 3 and 5. BARC: Bleeding Academic Research Consortium; CI: confidence interval; HR: hazard ratio

consistent with the matched analysis and are summarised in **Supplementary Table 3**.

In the univariate analysis, conventional risk factors, including age, hypertension, diabetes mellitus, chronic kidney disease, and low body mass index, were associated with an increased incidence of the primary endpoint events **(Table 3)**. A history of coronary bypass surgery, transfemoral approach, or left main disease was also associated with a higher incidence of the primary endpoint. In contrast, discontinuation of aspirin within 1 month had a protective effect against the occurrence of the primary endpoint. After covariate adjustment, discontinuing aspirin within 1 month remained an independent protective factor against the primary endpoint (HR 0.57, 95% CI: 0.38-0.86; p=0.007).

Figure 3 shows the subgroup analyses of the primary endpoint. The effect of aspirin discontinuation within 1 month versus at 3 months appeared consistent across clinically relevant subgroups. However, the number of events within each subgroup was limited, and these analyses should be considered exploratory.

Discussion

This study directly compared two aspirin discontinuation strategies (<1 month vs at 3 months) using individual patient data from two clinical trials. The main findings were as follows: (1) discontinuing aspirin within 1 month after PCI demonstrated superior net clinical benefits compared with discontinuation at 3 months; (2) the reduction in net clinical adverse events was primarily driven by a lower incidence of major bleeding, and ischaemic event rates were comparable between the groups; (3) the 3-month landmark analysis showed that events occurred more frequently during the first 90 days in the 3-month group, without significant heterogeneity between the early and late periods; and (4) discontinuing aspirin within 1 month was identified as an independent protective factor against the occurrence of the primary endpoint. The overall study design and main findings are summarised in the **Central illustration**.

Our findings provide insights into the optimal timing of aspirin discontinuation after short-term DAPT in patients with ACS. The benefits of the shorter duration of aspirin (<1 month) combined with ticagrelor monotherapy may be attributable to the increased bleeding risk associated with the concomitant use of aspirin and ticagrelor. Notably, ticagrelor inhibits thromboxane pathways, potentially diminishing the incremental antiplatelet effect of aspirin[17]. However, the optimal duration of concomitant aspirin use with potent $P2Y_{12}$ inhibitors remains uncertain.

In our 3-month landmark analysis, the direction of effect for both major adverse cardiac and cerebrovascular events and major bleeding was consistently unfavourable for the 3-month group across both periods, with statistically significant excess

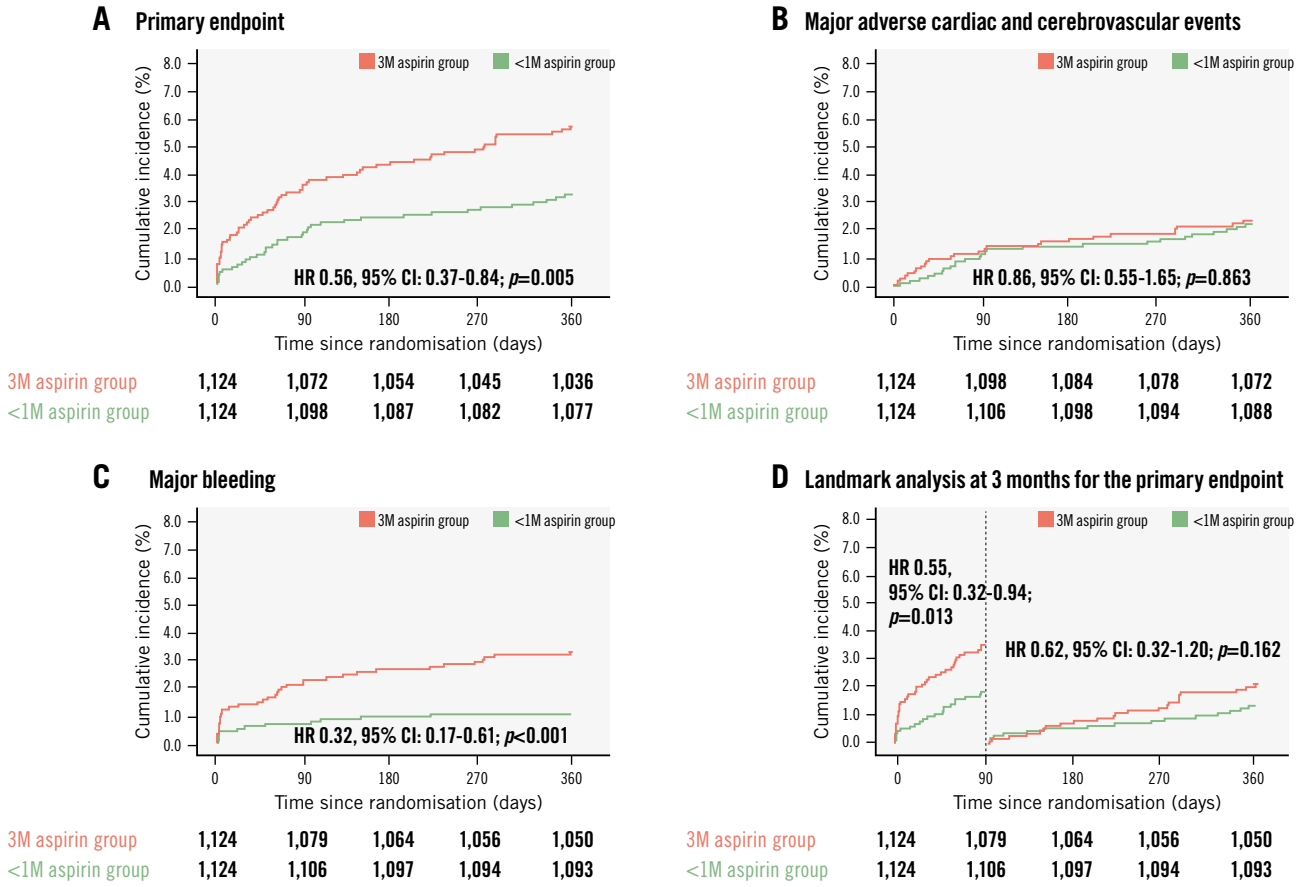


Figure 2. *Time-to-event curves for each clinical outcome in the propensity score-matched population. A) The <1-month aspirin discontinuation group showed a lower incidence of the primary endpoint (net adverse clinical events, defined as a composite of all-cause mortality, myocardial infarction, stent thrombosis, ischaemia-driven target vessel revascularisation, stroke, and major bleeding) than the 3-month discontinuation group. B) MACCE was defined as a composite of all-cause death, myocardial infarction, stent thrombosis, ischaemia-driven target vessel revascularisation, and stroke; MACCE rates were similar between the groups. C) Major bleeding, defined as BARC Type 3 or 5, was significantly lower in the <1-month aspirin discontinuation group compared with the 3-month group. D) A 3-month landmark analysis demonstrated that the excess risk in the 3-month group was confined to the first 90 days, whereas event rates between days 91 and 360 were not significantly different between the groups. 1M: 1 month; 3M: 3 months; BARC: Bleeding Academic Research Consortium; CI: confidence interval; HR: hazard ratio; MACCE: major adverse cardiac and cerebrovascular events*

risk confined to the first 90 days. This finding aligns with the biological plausibility that the concomitant use of aspirin and ticagrelor confers an increased risk of bleeding during the early treatment phase. In contrast, the transition to ticagrelor monotherapy attenuates this excess risk. Although the interaction testing was underpowered and the relatively small number of events limited the precision of our estimates, the absence of a significant interaction supports the overall consistency of the treatment effect across time periods.

Our study provides evidence to inform the optimal duration of aspirin therapy in combination with a potent $P2Y_{12}$ inhibitor, balancing ischaemic and bleeding risks. Several randomised trials have proposed similar objectives, investigating the efficacy and safety of reduced durations of potent $P2Y_{12}$ inhibitor-based DAPT and $P2Y_{12}$ inhibitor monotherapy in patients with ACS[18-21]. In particular, the Percutaneous Coronary Intervention Followed by Monotherapy Instead of Dual Antiplatelet Therapy in the Setting of Acute Coronary Syndromes (NEO-MINDSET) and Less Bleeding by Omitting Aspirin in non-ST-segment Elevation Acute Coronary Syndrome Patients (LEGACY) trials are designed to evaluate the impact of immediate aspirin discontinuation[19,20], whereas the Evaluation of a Modified Anti-Platelet Therapy Associated With Low-dose DES Firehawk in Acute Myocardial Infarction Patients Treated With Complete Revascularization Strategy (TARGET-FIRST) trial aimed to assess $P2Y_{12}$ inhibitor monotherapy after 1-month DAPT[21]. Moreover, beyond the early post-PCI phase, a recent individual patient data meta-analysis demonstrated that $P2Y_{12}$ inhibitor monotherapy was superior to aspirin monotherapy for long-term secondary prevention after PCI[22]. These findings reinforce the broader clinical relevance of $P2Y_{12}$ inhibitor-based strategies across both early and late phases of secondary prevention.

Table 3. Predictors for the 1-year primary endpoint in the propensity score-matched population.

	Univariate analysis		Multivariate analysis	
	HR (95% CI)	*p*-value	HR (95% CI)	*p*-value
Age, years	1.021 (1.002-1.041)	0.030	1.000 (0.979-1.022)	0.979
Male	1.370 (0.865-2.170)	0.179		
Body mass index, kg/m^2	0.881 (0.825-0.942)	<0.001	0.879 (0.979-1.022)	<0.001
Hypertension	1.444 (0.969-2.151)	0.071	1.326 (0.867-2.028)	0.193
Diabetes mellitus	1.835 (1.228-2.741)	0.003	1.534 (1.000-2.355)	0.049
Chronic kidney disease	2.615 (1.652-4.142)	<0.001	1.883 (1.125-3.151)	0.016
End-stage kidney disease on dialysis	4.780 (1.515-15.084)	0.008	1.084 (0.298-3.943)	0.903
Dyslipidaemia	0.832 (0.552-1.253)	0.378		
Current smoker	0.766 (0.503-1.168)	0.216		
Prior myocardial infarction	1.259 (0.399-3.972)	0.695		
Prior percutaneous coronary intervention	1.322 (0.688-2.542)	0.403		
Prior coronary artery bypass graft surgery	6.640 (1.637-26.931)	0.008	3.168 (0.749-13.399)	0.117
Prior stroke	0.856 (0.271-2.702)	0.791		
Admission via emergency department	1.161 (0.733-1.838)	0.525		
Acute MI presentation	1.137 (0.713-1.813)	0.589		
Transfemoral approach	1.759 (1.186-2.610)	0.005	1.669 (1.117-2.492)	0.012
Multivessel disease	1.407 (0.936-2.113)	0.101		
Left main disease	3.225 (1.412-7.362)	0.005	2.746 (1.156-6.523)	0.022
Bifurcation disease	0.995 (0.515-1.724)	0.986		
<1-month aspirin discontinuation[a]	0.560 (0.372-0.844)	0.006	0.569 (0.377-0.857)	0.007

[a]3-month aspirin discontinuation as the reference. CI: confidence interval; HR: hazard ratio; MI: myocardial infarction

In our analysis, compared with the 3-month group, the lower incidence of major bleeding in the <1-month group was the driving factor for the reduction in net clinical adverse events. Major bleeding events during the acute phase of ACS treatment significantly increase the risk of mortality. These events are associated with haemodynamic instability or shock, which can lead to myocardial ischaemia[23]. Furthermore, red blood cell transfusions may increase platelet activation and aggregation[24]. In this context, the following DAPT de-escalation strategies have recently emerged to achieve an optimal balance between ischaemic and bleeding risk: (1) switching from a potent $P2Y_{12}$ inhibitor to a less potent one[25,26], (2) reducing the dose of prasugrel or ticagrelor[27], and (3) discontinuing one of the two antiplatelet agents. Among these strategies, the TICO and T-PASS trials evaluated the clinical efficacy and safety of aspirin discontinuation in an abbreviated ticagrelor-based DAPT in patients with ACS[9,10].

Our study is consistent with previous research showing that abbreviated aspirin therapy followed by ticagrelor monotherapy reduces bleeding events and improves net clinical outcomes. Prespecified subgroup analyses from randomised clinical trials on ticagrelor monotherapy for the treatment of ACS have consistently shown a significant reduction in major bleeding without an increase in ischaemic risk[28,29]. Similarly, a patient-level meta-analysis of randomised clinical trials in patients with ACS suggested that short-term DAPT was associated with reduced major bleeding without an increase in ischaemic events[30]. The TARGET-FIRST trial demonstrated that at least 1 month of DAPT followed by $P2Y_{12}$ inhibitor monotherapy reduced bleeding risk without increasing ischaemic event rates[31], whereas the NEO-MINDSET trial found that immediate aspirin discontinuation may be harmful in terms of ischaemic risk[32]. Taken together with our findings, these recent study results suggest that a short duration of aspirin therapy plays an important role in balancing bleeding and ischaemic risks.

As the duration of DAPT has been shortened to reduce bleeding complications, concerns have emerged regarding recurrent ischaemic events, including stent thrombosis and myocardial infarction, especially in patients presenting with ACS. The Smart Angioplasty Research Team: Safety of Six-Month Duration of Dual Antiplatelet Therapy After Percutaneous Coronary Intervention in Patients With Acute Coronary Syndromes (SMART-DATE) trial indicated that a 6-month DAPT duration was associated with a higher risk of myocardial infarction than the standard 12-month duration in patients with ACS[33]. However, this trial predominantly used clopidogrel (80.8%) instead of a more potent $P2Y_{12}$ inhibitor, such as prasugrel or ticagrelor, as recommended in the current ACS guidelines.

The Short and Optimal Duration of Dual Antiplatelet Therapy After Everolimus-Eluting Cobalt-Chromium Stent-3 (STOPDAPT-3) trial investigated an aspirin-free strategy using low-dose prasugrel initiated immediately after PCI[34]. This approach was associated with increased ischaemic events and failed to reduce bleeding risk, suggesting that aspirin may still

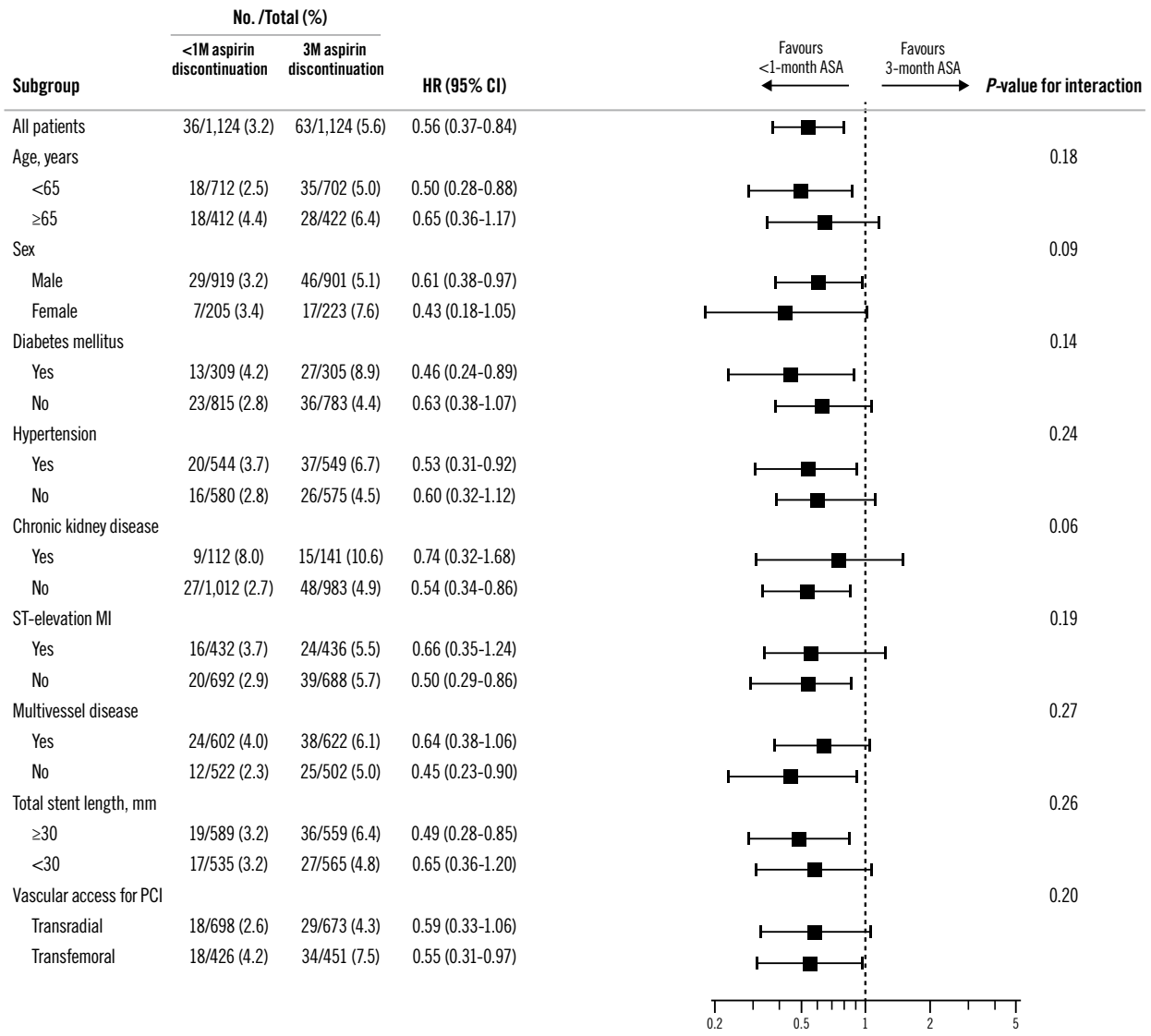


Figure 3. *Subgroup analyses for the primary endpoint in the propensity score-matched population. 1M: 1 month; 3M: 3 months; ASA: acetylsalicylic acid (aspirin); CI: confidence interval; HR: hazard ratio; MI: myocardial infarction; PCI: percutaneous coronary intervention*

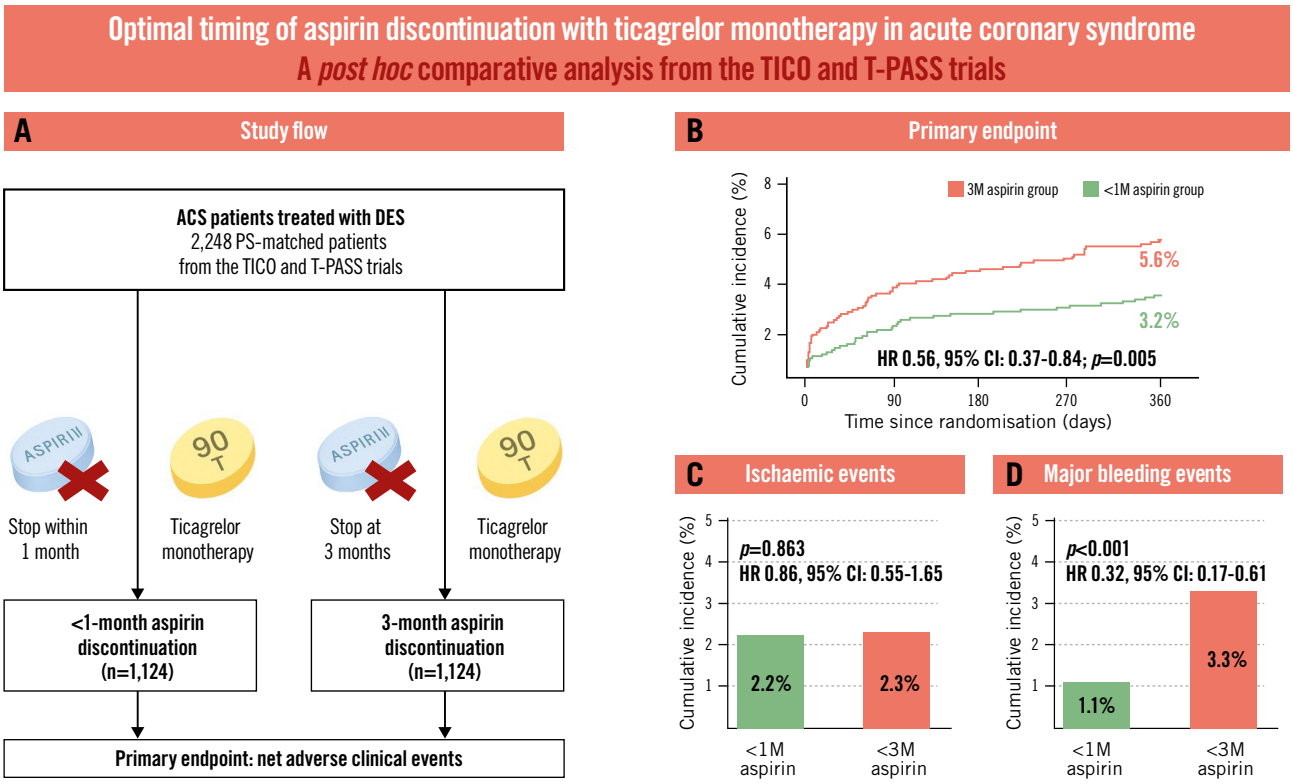
play a protective role during the immediate periprocedural period. In this context, our study holds clinical significance by evaluating the efficacy and safety of different aspirin discontinuation durations, while maintaining a consistent ticagrelor-based antiplatelet strategy. Our findings suggest that early aspirin discontinuation with ticagrelor monotherapy may offer a favourable balance between bleeding and ischaemic risks in patients with ACS undergoing PCI.

A recent individual patient data meta-analysis that included the TICO and T-PASS trials compared ticagrelor monotherapy after short-term DAPT with conventional 12-month DAPT[35]. The study demonstrated that de-escalation to ticagrelor monotherapy reduced major bleeding without increasing ischaemic risk. However, in a prespecified subgroup analysis, the timing of aspirin discontinuation (≤30 vs >30 days) was not associated with differences in clinical outcomes[35]. In contrast, our study directly compared <1-month and 3-month discontinuation strategies and identified a significant difference in bleeding risk. These divergent findings highlight the need for prospective randomised trials specifically designed to determine the optimal timing of aspirin withdrawal in patients with ACS undergoing PCI.

Limitations

Our study had certain limitations. First, although the study used individual patient-level data from two randomised trials, the comparison between <1-month and 3-month aspirin discontinuation was *post hoc*, cross-trial, and observational, without randomisation. Propensity score matching was performed to minimise the influence of baseline differences; however, residual confounding is

Aspirin discontinuation within 1 month versus at 3 months with ticagrelor monotherapy in acute coronary syndrome.



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A) Study flow. Cumulative incidences of the primary endpoint (B), ischaemic events (C), and major bleeding events (D). 1M: 1 month; 3M: 3 months; ACS: acute coronary syndrome; CI: confidence interval; DES: drug-eluting stent; HR: hazard ratio; PS: propensity score; T-PASS: Ticagrelor Monotherapy in PAtients Treated With New-generation Drug-eluting Stents for Acute Coronary Syndrome; TICO: Ticagrelor Monotherapy After 3 Months in the Patients Treated With New Generation Sirolimus Stent for Acute Coronary Syndrome

inevitable, and the results should be interpreted with caution. International guidelines at the time these trials were initiated recommended 12 months of DAPT with aspirin and a potent $P2Y_{12}$ inhibitor as the standard of care for ACS. Thus, our pooled analysis provides important indirect evidence, and a dedicated randomised trial directly comparing <1-month versus 3-month discontinuation strategies is warranted. Second, as a *post hoc* pooled analysis of individual patient data from previous trials, differences in baseline characteristics were observed because of the different periods in which the trials were conducted. In addition, within the <1-month group, the actual timing of aspirin discontinuation varied throughout the first month. This variability may have introduced heterogeneity, limiting the precision of the treatment effect. Third, both the TICO and T-PASS trials were conducted in the Republic of Korea, which limits the generalisability of our findings to Western populations. East Asian populations may exhibit different ischaemic and bleeding tendencies than Caucasian populations; consequently, our results should be confirmed in Western populations. Fourth, we only extended follow-up to 1 year, which may not reflect long-term clinical outcomes. Lastly, these trials exclusively included patients who received biodegradable-polymer sirolimus-eluting stents, potentially limiting the applicability of our findings to patients treated with other types of stents.

Conclusions

Aspirin discontinuation within 1 month after PCI, followed by ticagrelor monotherapy, demonstrated superior net clinical benefits compared with discontinuation at 3 months. These benefits were primarily driven by a significant reduction in major bleeding, without an increase in ischaemic events. Therefore, aspirin discontinuation within 1 month followed by ticagrelor monotherapy may be considered a feasible strategy in patients with ACS treated with DES.

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Conflict of interest statement

The authors have no conflicts of interest to declare.

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Supplementary data

Supplementary Table 1. Inclusion and exclusion criteria of the TICO and T-PASS trials.

Supplementary Table 2. Clinical, angiographic, and procedural characteristics in the overall population.

Supplementary Table 3. Clinical outcomes at 1 year in the overall population.

Data sharing statement.

The supplementary data are published online at: https://eurointervention.pcronline.com/doi/10.4244/EIJ-D-25-00832

Supplementary data

Supplementary Table 1. Inclusion and exclusion criteria of the TICO and T-PASS trials.

Criteria	TICO Trial	T-PASS Trial
Inclusion	1. Age ≥19 years	1. Age ≥19 years
	2. Patients who received bioresorbable polymer sirolimus-eluting stent implantation to treat acute coronary syndrome	2. Patients who received new-generation sirolimus-eluting stent implantation for treating acute coronary syndrome.
	3. Provision of informed consent	3. Provision of informed consent
Exclusion	1. Age >80 years	1. Age >80 years
	2. Increased risk of bleeding due to: 1) Any prior event of hemorrhagic stroke; 2) Ischemic stroke, dementia, or impairment of central nervous system within a year; 3) Traumatic brain injury or brain surgery within the past 6 months; 4) Known intracranial tumor; 5) Documented or suspected aortic dissection; 6) Internal bleeding within the past 6 weeks; 7) Active bleeding or bleeding diathesis; 8) Anemia (hemoglobin ≤8 g/dL) or thrombocytopenia (platelet count < 100,000/μL); and 9) Major surgery or traumatic injury resulting in any impairment of physical activity within the past 3 weeks	2. Increased risk of bleeding, anemia, and thrombocytopenia
	3. Need for oral anticoagulation therapy	3. A need for oral anticoagulation therapy
		4. Pregnant women or women with potential childbearing
		5. Life expectancy < 1 year

	4. Current or potential pregnancy 5. Life expectancy <1 year 6. Currently treated with strong cytochrome P4503A4 inhibitors 7. Moderate to severe hepatic dysfunction (Child-Pugh class B or C) 8. Increased risk of bradycardia-related symptoms

Supplementary Table 2. Clinical, angiographic, and procedural characteristics in the overall population.

	< 1-month aspirin discontinuation (n=1,426)	**3-month aspirin discontinuation (n=1,527)**	**p-value**
Age (years)	60.6±10.5	60.7±10.8	0.872
Male	1,193 (83.7)	1,204 (78.8)	0.001
Body mass index (kg/m^2)	25.1±3.6	24.9±3.2	0.207
Hypertension	669 (46.9)	760 (49.8)	0.121
Diabetes mellitus	422 (29.6)	418 (27.4)	0.182
Diabetes mellitus with insulin	40 (2.8)	42 (2.8)	0.928
Chronic kidney disease [a]	118 (8.3)	292 (19.1)	<0.001
End-stage kidney disease on dialysis	11 (0.8)	10 (0.7)	0.707
Dyslipidemia	1,048 (73.5)	924 (60.5)	<0.001
Current smoker	557 (39.1)	555 (36.3)	0.128
Prior myocardial infarction	27 (1.9)	64 (4.2)	<0.001
Prior percutaneous coronary intervention	92 (6.5)	135 (8.8)	0.015
Prior coronary bypass graft surgery	4 (0.3)	8 (0.5)	0.299
Prior stroke	43 (3.0)	60 (3.9)	0.176
Clinical presentation			0.008
Unstable angina	347 (24.3)	442 (28.9)	
Non ST-elevation MI	507 (35.6)	539 (35.3)	
ST-elevation MI	572 (40.1)	546 (35.8)	
Transradial approach	959 (67.3)	837 (54.8)	<0.001
Use of IABP	21 (1.5)	17 (1.1)	0.387
Use of ECMO	6 (0.4)	4 (0.3)	0.458
Multi-vessel disease	749 (52.5)	842 (55.1)	0.154
Left main disease	23 (1.6)	71 (4.6)	<0.001
Bifurcation disease	219 (15.4)	255 (16.7)	0.321
Use of glycoprotein IIb/IIIa inhibitors	93 (6.5)	100 (6.5)	0.976
Use of thrombectomy	79 (5.5)	68 (4.5)	0.175
Multi-lesion intervention	299 (21.0)	306 (20.0)	0.532
Multi-vessel intervention	233 (16.3)	253 (16.6)	0.867
Treated lesions per patient	1.0 (1.0-1.0)	1.0 (1.0-1.0)	0.531

Total number of stents per patient	1.0 (1.0-2.0)	1.0 (1.0-2.0)	0.044
Total stent length per patient (mm)	30.0 (22.0-48.0)	26 (22.0-40.0)	<0.001

Data are reported as No. (%) unless otherwise indicated

[a] Chronic kidney disease was defined as an estimated glomerular filtration rate of less than 60mL/min/1.73 m^2 of body surface area.

MI, myocardial infarction; IABP, intra-aortic balloon pump; ECMO, extracorporeal membrane oxygenation

Supplementary Table 3. Clinical outcomes at 1 year in the overall population.

	< 1-month aspirin discontinuation (n=1,426)	3-month aspirin discontinuation (n=1,527)	HR (95% CI)	p-value
Primary endpoint				
Net adverse clinical event [a]	48 (3.4)	82 (5.4)	0.61 (0.43–0.88)	0.007
Secondary endpoints				
Major adverse cardiac and cerebrovascular event [b]	34 (2.4)	33 (2.2)	1.09 (0.68–1.75)	0.719
Major bleeding [c]	17 (1.2)	53 (3.5)	0.34 (0.20–0.58)	<0.001
BARC type 3	15 (1.1)	53 (3.5)	0.33 (0.19–0.58)	<0.001
BARC type 5	2 (0.1)	0 (0.0)	-	0.151
Cardiac death, myocardial infarction, or stroke	19 (1.3)	21 (1.4)	0.96 (0.52–1.79)	0.897
All-cause death	14 (1.0)	16 (1.0)	0.93 (0.45–1.89)	0.839
Cardiac death	6 (0.4)	7 (0.5)	0.91 (0.31–2.70)	0.865
Myocardial infarction	7 (0.5)	6 (0.4)	1.23 (0.42–3.70)	0.699
Stent thrombosis	2 (0.1)	6 (0.4)	0.35 (0.07–1.75)	0.185
Subacute	2	4	-	
Late	0	2	-	
Stroke	8 (0.6)	8 (0.5)	1.06 (0.40–2.86)	0.908
Ischemic	6	5	-	
Hemorrhagic	2	3	-	
Ischemia-driven target-vessel revascularization	11 (0.8)	6 (0.4)	1.92 (0.71–5.26)	0.185

Data are presented for the intention-to-treat population and number of patients with event (% are Kaplan-Meier estimates at day 360).

[a] Net adverse clinical event included the composite of major adverse cardiac and cerebrovascular events and major bleeding.

[b] Major adverse cardiac and cerebrovascular event included the composite of all-cause death, myocardial infarction, stent thrombosis, ischemia-driven target-vessel revascularization and stroke.

[c] Major bleeding included the composite of BARC type 3 and 5.

BARC, Bleeding Academic Research Consortium

Data sharing statement

The data supporting the findings of this study will be shared by the corresponding author upon reasonable request.