Interruption of Dual Antiplatelet Therapy Within Six Months After Coronary Stents (from the Dual Antiplatelet Therapy Study)

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The risk of major adverse cardiac and cerebrovascular events (MACCE) in subjects who interrupt temporarily or permanently thienopyridine therapy in the first 6 months after percutaneous coronary intervention (PCI) remains uncertain. In the dual antiplatelet therapy (DAPT) study subjects were enrolled within 72 hours of PCI and treated with aspirin and a thienopyridine for 12 months before being randomized to continued thienopyridine versus placebo. This analysis focuses on the 12-month period before randomization. Thienopyridine interruptions of greater than 24 hours, occurring in the first 6 months after PCI were evaluated. The incidence of MACCE and moderate or severe bleeding occurring within 12 months after PCI were compared between subjects with and without interruptions. Among 23,002 subjects, the incidence of interruption of thienopyridine was 5.1% (n = 1,173). Compared with subjects who adhered to treatment, subjects with an interruption had a higher incidence of MACCE (6.1% vs 4.3%, p = 0.005), death (2.2% vs 1.4%, p = 0.02), myocardial infarction (3.8% vs 2.7%, p = 0.03), and bleeding (3.1% vs 2.2%, p = 0.04) at 12 months. After adjusting for baseline characteristics, interruptions were associated with MACCE (adjusted odds ratio 1.3, 95% confidence interval 1.0, 1.7, p = 0.04) and had a borderline association with subsequent bleeding (adjusted odds ratio 1.4, 95% confidence interval 1.0, 2.0, p = 0.05). In conclusion, interruption of thienopyridine in the first 6 months after PCI occurs not infrequently and is associated with an increased risk of MACCE and subsequent bleeding between the time of interruption and 12 months after PCI. **(Am J Cardiol 2019;124:1813−1820)**

Although continuation of thienopyridine and aspirin beyond 1 year after coronary stent procedures for stable angina or acute coronary syndromes (ACS) has been demonstrated to reduce late risks of major adverse cardiac and cerebrovascular events (major adverse cardiac and cerebrovascular events [MACCE]; death, myocardial infarction [MI], or stroke) and MI in randomized trials, it also increases bleeding risk.[1] Because the risks of bleeding and ischemia may differ between patients, clinical tools have been proposed to individualize treatment.[2,3] Meanwhile several studies have suggested that with new generation drug-eluting stents, the risk of thrombotic events is not increased even with 1 to 6 months of dual antiplatelet therapy. These studies, however, have been limited in size, open label (and therefore susceptible to bias), included substantial crossover rates between treatment arms[4] and have, therefore, been inconclusive regarding noninferiority of ischemic risk.[5−8] Observational studies have demonstrated variable increased risk of death or MI, stent thrombosis, or repeat revascularization with interruption in the first 6 months.[9−11] Subjects enrolled in the dual antiplatelet therapy (DAPT) Study were considered to be eligible for DAPT continuation for at least 12 months, though some patients interrupted temporarily or permanently thienopyridine therapy before 12 months. We sought to estimate the incidence of interruptions (temporary or permanent) of thienopyridine occurring in the first 6 months after percutaneous coronary intervention (PCI), to assess the predictors and events leading to interruption, and to evaluate the association of interruption with subsequent ischemic and bleeding events.

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See page 1819 for disclosure information.

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Methods

Subjects over the age of 18 with either stable angina pectoris or an ACS, able to give informed consent, and meeting all inclusion and exclusion criteria[12] were enrolled in the DAPT Study within 72 hours of undergoing PCI with a drug-eluting or bare metal coronary stent if they were deemed eligible to be treated with DAPT for more than 12 months. They received open-label thienopyridine (clopidogrel or prasugrel) and aspirin for the first 12 months after enrollment, at which point eligible subjects entered in the randomized phase of the DAPT Study. Subjects not eligible for randomization were followed for the full 12-month period, with the exception of subjects enrolled into one substudy which were allowed to exit the study after sustaining a disqualifying ischemic or bleeding event before a protocol amendment in 2011. Full details of the study design have been previously published.[1,12] In this analysis, all enrolled subjects who were followed for at least 330 (=360 days minus the allowable 30-day window in which to attend the 360 day visit) days after PCI, or who had a study end point within 360 days after PCI, were included. In a secondary analysis, only subjects with per-protocol planned follow-up to 12 months were included. Interruptions of at least 24 hours (whether therapy was resumed or not) of thienopyridine by 6 months after enrollment were assessed. Ischemic or bleeding events for all subjects were adjudicated by an independent clinical events committee and were assessed for the 12-month period after PCI; in patients with interruptions, only subsequent occurrence of ischemic or bleeding events after the interruption were considered an end point. Timing and cause for interruptions of thienopyridine therapy were assessed at the 6-month study visit. Additional manual review of source documents was performed for subjects who had an interruption and an adjudicated ischemic or bleeding end point in the first 12 months to determine the date, length, and reason of the interruption. Source documents were not available for review in the absence of a clinical event. Changes in thienopyridine regimen (dose or medication type) that did not result in an interruption in therapy of more than 24 hours were not considered to be interruptions. The study was approved by the institutional review board at each site. The primary end point of interest for this analysis was the occurrence of MACCE. Secondary end points included all-cause death, MI, Academic Research Consortium definite or probable stent thrombosis (ST),[13] stroke, and Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Arteries (GUSTO) moderate or severe bleeding.[14]

The incidence of adverse events (MACCE, MI, and bleeding) occurring after an interruption were compared with the incidence of events over the 12 months observational period in subjects without interruptions by Fisher's exact test. Baseline demographics were compared using the Student's *t* test for continuous variables. Multivariate logistic regression models were built to evaluate predictors of interruptions of thienopyridine, as well as adjusted risk of MACCE and MI within the first 12 months after PCI in those with or without interruptions. Candidate variables were entered in the model if $p = 0.2$, and were kept if they met a criterion of $p = 0.1$ (Supplemental Table 1). Rates of thienopyridine interruption and association with subsequent outcomes were also compared between DAPT Score groups (< or ≥2).[2] Subjects with a DAPT Score ≥2 have a higher predicted anti-ischemic benefit (reduction in MI and ST) without a significant increase in GUSTO moderate or severe bleeding events, when continuing DAPT beyond 1 year after PCI, whereas subjects with a DAPT Score <2 had a higher bleeding risk without significant anti-ischemic benefit. Statistical analyses were conducted at the Baim Institute for Clinical Research, with SAS software version 9.4 (SAS Institute Inc., Cary, North Carolina). A 2-sided p value of ≤0.05 was considered significant for all analyses.

Results

Of the 25,682 subjects enrolled in the DAPT Study, 23,002 had either complete 12-month follow-up or a MACCE or bleeding event and were eligible for this study. Patient and procedural characteristics are presented in Table 1. Over the 12-month study period, the incidence of MACCE was 4.4%, MI 2.8% (of which 16.9% had ST-related MI), death 1.4%, stroke 0.7%, and GUSTO moderate or severe bleeding 2.2%. In the first 6 months after enrollment, 1,173 (5.1%) subjects had at least 1 interruption or discontinued thienopyridine therapy. In the population of 12,976 subjects who were enrolled with protocol-driven follow-up to 12 months, 650 (5.0%) had an interruption or discontinued therapy. The independent predictors of interruption included having a bare-metal stent, not presenting with ACS, enrollment in North America, and current tobacco use (Table 2). In all subjects with interruption, a GUSTO moderate or severe bleeding event before interruption occurred in 102 subjects (8.7%), whereas an MI was present in 38 (3.2%), and stroke in 22 (1.9%). In the 239 subjects who had an interruption and a MACCE or bleeding event at any time during follow-up, source documents indicated any bleeding as the most commonly identified reason for the interruption (48%), followed by nonadherence (19%), need for surgery (16%), other specified reasons (8%), and unknown (10%). In that same group of patients, 18% of subjects had interruptions shorter than 5 days, 31% had interruptions between 5 and 14 days, 19% had interruptions for more than 14 days, 29% had permanent interruptions (discontinuation), and 2.5% had interruptions of unknown duration.

In the population of all patients with 12 months of follow-up or intervening events, the incidence of subsequent MACCE was higher in subjects with interruption of thienopyridine compared with subjects without interruption (6.1% vs 4.3%, $p = 0.005$, adjusted $p = 0.037$) (Figure 1). Interruption was associated with unadjusted odds of MACCE of 1.4 (95% confidence interval [CI] 1.1, 1.9, $p = 0.004$) and remained a significant predictor of MACCE (odds ratio [OR] 1.3, 95% CI [1.0, 1.7], $p = 0.037$), after adjusting for comorbidities, baseline PCI characteristics, stent type (paclitaxel-eluting, other drug-eluting, and bare-metal stents), and DAPT Score group (Table 3). In the subgroup of subjects with an interruption, the significant predictors of subsequent MACCE were older age, previous PCI, and renal insufficiency; previous MI was borderline and added to the model (Table 4). The incidences of subsequent MACCE, MI or ST, and bleeding after thienopyridine interruption were similar between subjects who interrupted at different times in the first 6 months after initial PCI.

Table 1
Baseline and procedural characteristics

Variable	Interruption of thienopyridine 0-6 months after percutaneous coronary intervention		p Value
	Yes (n = 1,173 patients)	No (n = 21,829 patients)	
Age, years,			
Mean ± standard deviation	62.4 ± 10.7	62.0 ± 10.6	0.208
Women	357 (30.4%)	6,019 (27.6%)	0.035
Nonwhite	130 (11.4%)	2,126 (9.9%)	0.116
Body mass index (Kg/m^2)			
Mean ± standard deviation	30.6 ± 6.3	30.4 ± 5.8	0.256
Diabetes mellitus	423 (36.1%)	6,879 (31.6%)	0.001
Hypertension	891 (76.2%)	16,745 (76.9%)	0.569
Cigarette smoking (within past year)	334 (28.8%)	5,782 (26.8%)	0.144
Previous myocardial infarction	274 (24.1%)	4,967 (23.2%)	0.471
Previous percutaneous coronary intervention	418 (35.9%)	7,219 (33.2%)	0.069
Coronary bypass	203 (17.3%)	2,851 (13.1%)	<0.001
Stroke/transient ischemic attack	65 (5.6%)	919 (4.2%)	0.031
Congestive heart failure	104 (8.9%)	1,306 (6.0%)	<0.001
Peripheral arterial disease	113 (9.9%)	1,440 (6.7%)	<.001
Indication for Index Procedure			
Acute coronary syndrome	283 (24.1%)	5,972 (27.4%)	0.015
ST-elevation myocardial infarction	100 (8.5%)	2,628 (12.0%)	<0.001
Non ST-elevation myocardial infarction	183 (15.6%)	3,344 (15.3%)	0.803
Unstable angina pectoris	207 (17.7%)	3,661 (16.8%)	0.446
Stable angina pectoris	435 (37.1%)	7,879 (36.1%)	0.493
Other	248 (21.1%)	4,317 (19.8%)	0.260
Region			<0.001
North America	1,081 (92.2%)	19,805 (90.7%)	
Europe	52 (4.4%)	1,669 (7.7%)	
Australia, New Zealand	40 (3.4%)	355 (1.6%)	
Thienopyridine drug at start of open-label period			
Clopidogrel	817 (69.7%)	15,559 (71.5%)	0.185
Prasugrel	347 (29.6%)	6,227 (28.5%)	0.446
Drug-eluting stent type			
Everolimus-eluting	481 (47.5%)	9,551 (48.7%)	0.458
Paclitaxel-eluting	215 (21.3%)	4,382 (22.4%)	0.416
Zotarolimus-eluting	170 (16.8%)	2,803 (14.3%)	0.031
Sirolimus-eluting	116 (11.5%)	2,386 (12.2%)	0.521
>1 type	30 (3.0%)	475 (2.4%)	0.296
Bare-metal stent	161 (13.7%)	2,231 (10.2%)	<0.001
Number of treated lesions (per patient), mean ± standard deviation	1.3 ± 0.5	1.3 ± 0.6	0.397
Number of treated vessels (per patient), mean ± standard deviation	1.1 ± 0.3	1.1 ± 0.3	0.968
Number of stents (per patient)			
Mean ± standard deviation	1.5 ± 0.7	1.5 ± 0.8	0.064
Minimum stent diameter (mm)			0.239
≥3.0	655 (55.8%)	11,805 (54.1%)	
<3.0	518 (44.2%)	10,024 (45.9%)	
Total stent length (per patient), mm, mean ± standard deviation	27.6±16.5	28.0 ± 17.6	0.427
Vessel type			
Native coronary	1,453 (95.4%)	27,681 (96.5%)	0.027
Left main	24 (1.6%)	304 (1.1%)	0.074
Left anterior descending	551 (36.2%)	11,227 (39.1%)	0.022
Right coronary artery	516 (33.9%)	9,604 (33.5%)	0.759
Left circumflex artery	362 (23.8%)	6,545 (22.8%)	0.398
Venous graft	60 (3.9%)	859 (3.0%)	0.046
Arterial graft	10 (0.7%)	141 (0.5%)	0.349
In-stent restenosis	76 (5.0%)	1,310 (4.6%)	0.451
Extreme tortuosity	86 (5.7%)	1,268 (4.5%)	0.030
Heavy calcium	122 (8.1%)	2,412 (8.5%)	0.635
Modified ACC/AHA lesion Class B2 or C	658 (45.7%)	12,214 (44.9%)	0.550
DAPT score			
DAPT <2	566 (48.3%)	10,611 (48.6%)	0.834
DAPT ≥2	607 (51.8%)	11,218 (51.4%)	0.834

DAPT = Dual antiplatelet therapy study.

Table 2
Multivariate predictors of interruptions of thienopyridine in the first 6 months after percutaneous coronary intervention

Variable	Odds ratio [95% CI]	Adjusted p values
Bare-metal stent vs drug-eluting stent	1.617 [1.342, 1.948]	<0.001
Prior coronary bypass	1.289 [1.096, 1.515]	0.002
History of congestive heart failure	1.352 [1.091, 1.675]	0.006
History of peripheral arterial disease	1.333 [1.085, 1.637]	0.006
Acute coronary syndrome within 72 hours of enrollment	0.817 [0.706, 0.945]	0.007
Diabetes mellitus	1.161 [1.024, 1.316]	0.020
Region: North America	1.277 [1.015, 1.605]	0.037
Current tobacco use	1.146 [1.001, 1.311]	0.048

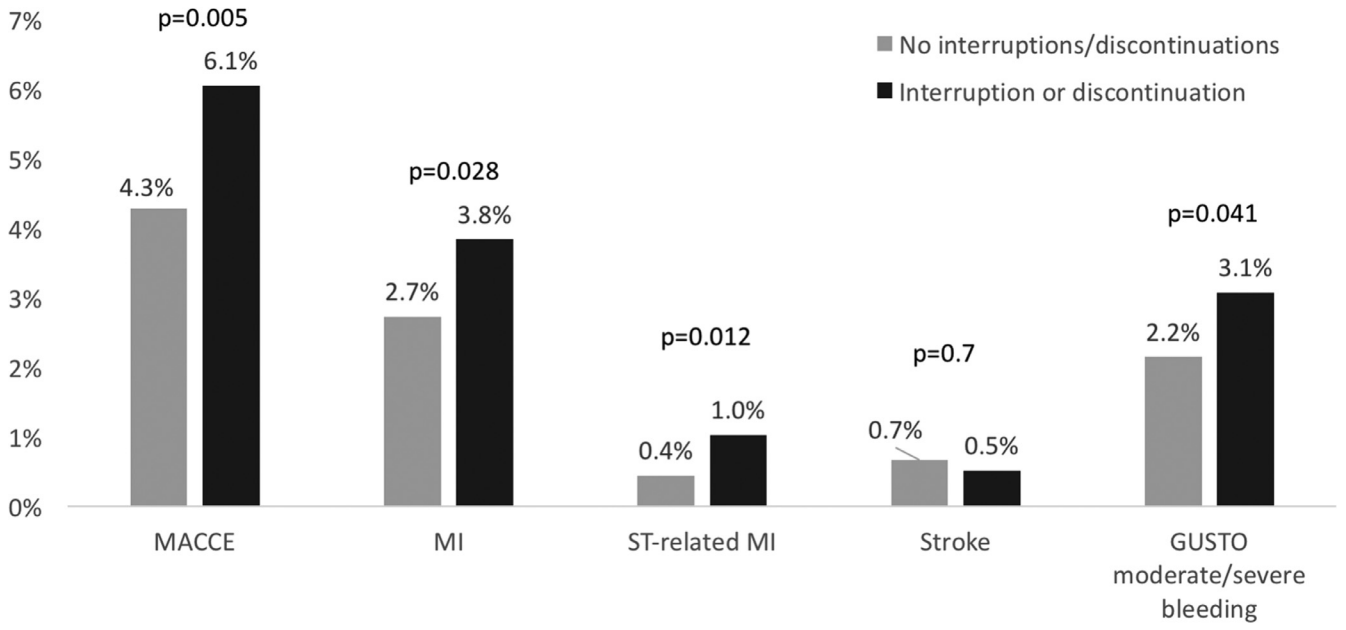

Figure 1. Incidence of adverse events in patients with versus without interruptions of thienopyridine (n = 23002). GUSTO = Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Arteries; MACCE = major adverse cardiac and cerebrovascular events; MI = myocardial infarction; ST = Stent thrombosis.

Table 3
Multivariate predictors of major adverse cardiac and cerebrovascular events

Variable	Odds ratio [95% CI]	Adjusted p values
Diabetes mellitus	1.767 [1.532, 2.037]	<0.001
Age ≥75 years	1.996 [1.659, 2.402]	<0.001
Renal insufficiency (creatinine ≥2.0 or dialysis)	1.991 [1.631, 2.431]	<0.001
Acute coronary syndrome within 72 hours of enrollment	1.565 [1.341, 1.827]	<0.001
Prior coronary bypass	1.619 [1.369, 1.914]	<0.001
Left ventricular ejection fraction <30%	2.130 [1.579, 2.873]	<0.001
Man	0.718 [0.626, 0.824]	<0.001
Lesion length >= 30 mm	1.560 [1.293, 1.882]	<0.001
In-stent restenosis of a drug-eluting stent	1.699 [1.307, 2.207]	<0.001
White vs nonwhite race	0.707 [0.587, 0.853]	<0.001
>2 Lesions per vessel vs <= 2 lesions per vessel	1.753 [1.249, 2.459]	0.001
Prior percutaneous coronary intervention	1.273 [1.098, 1.477]	0.001
Current tobacco use	1.293 [1.101, 1.519]	0.002
Type of stent (paclitaxel-eluting stent vs non paclitaxel drug-eluting stent)	0.766 [0.640, 0.917]	0.004
Type of stent (bare-metal vs nonpaclitaxel drug-eluting stent)	1.286 [1.049, 1.578]	0.016
DAPT score <2 vs ≥2	0.807 [0.673, 0.969]	0.021
Interruption	1.313 [1.016, 1.696]	0.038
Percutaneous coronary intervention to >2 vessels vs ≤2 vessels	2.031 [0.967, 4.265]	0.061

Table 4
Multivariate predictors of subsequent major adverse cardiac and cerebrovascular events in subset of patients with an interruption

	Odds Ratio [95% CI]	Adjusted p values
Age ≥75 years	2.20 [1.21,4.01]	0.010
Prior percutaneous coronary intervention	1.92 [1.14,3.22]	0.013
Renal insufficiency	2.07 [1.03,4.17]	0.041
Prior myocardial infarction	0.52 [0.26,1.03]	0.059
Type of stent (paclitaxel-eluting stent vs nonpaclitaxel drug-eluting stent)	1.18 [0.64,2.18]	0.593
Type of stent (bare-metal vs non-paclitaxel drug-eluting stent)	0.91 [0.43,1.92]	0.804

The incidence of MI was higher in subjects with interruption (3.8% vs 2.7%, p = 0.03, Figure 1), but was no longer significant after adjustment (OR 1.3, 95% CI 0.9 to 1.8, p = 0.11). The incidence of subsequent GUSTO moderate or severe bleeding was also higher after an interruption (3.1% vs 2.2% in patients without interruption, p = 0.04); after adjustment, interruption was a borderline predictor of bleeding (OR 1.4, 95% CI 1.0 to 2.0, p = 0.054). The incidence of stroke was not significantly different between subjects with interruptions and those without (0.5% vs 0.7%, p = 0.7), whereas that of death was higher after interruption than in the participants without (2.2% vs 1.4%, p = 0.02). In subjects who interrupted thienopyridine and had subsequent events, the majority of events occurred in the first 3 months after interruption, with 32.4% of MACCE, 40% of MI or ST, and 47.2% of bleeding events occurring in the first month after the interruption (Figure 2). Similar trends, albeit with a smaller number of events, were seen in the 12,976 subjects with per-protocol planned follow-up to 12 months (Figure 3).

The interaction of DAPT score and interruption is shown in Table 5. The incidence of MI or ST was numerically higher in subjects with DAPT score ≥2 and interruption compared with no interruption (5.4% vs 3.8%, p = 0.069), but there was no significant interaction (p = 0.5). The incidence of bleeding was numerically but not significantly higher in both DAPT score groups. The incidence of all-cause mortality was significantly higher in subjects with DAPT score <2 and interruptions compared with those without interruption.

Discussion

In the observational portion of the DAPT study, 5.1% of subjects undergoing PCI and prescribed open label DAPT for 12 months, had an interruption or discontinued thienopyridine within 6 months. The incidence of subsequent MACCE, MI, and moderate/severe bleeding events was higher in subjects with interruptions compared with subjects without. As all subjects had been planned for 12 months of thienopyridine therapy after PCI, interruptions were unexpected and occurred in a high-risk subgroup with more co-morbidities. Nevertheless, after adjusting for these co-morbidities, stent type, and DAPT Score, an interruption in the first 6 months remained a significant predictor of subsequent MACCE. The PARIS (Patterns of non-Adherence to antiplatelet Regimens in Stented subjects) Registry assessed frequency, patterns, and risks of nonadherence to DAPT in an unselected cohort of 5,031 subjects followed for 2 years after PCI.[9] The rate of any interruption of DAPT was 2.9% at 30 days, and 23.3% at 12 months after PCI; a higher incidence of the composite of cardiac death, stent thrombosis, MI or target-lesion revascularization, was also noted in patients with unplanned disruptions in DAPT. A higher incidence of thienopyridine interruption has been

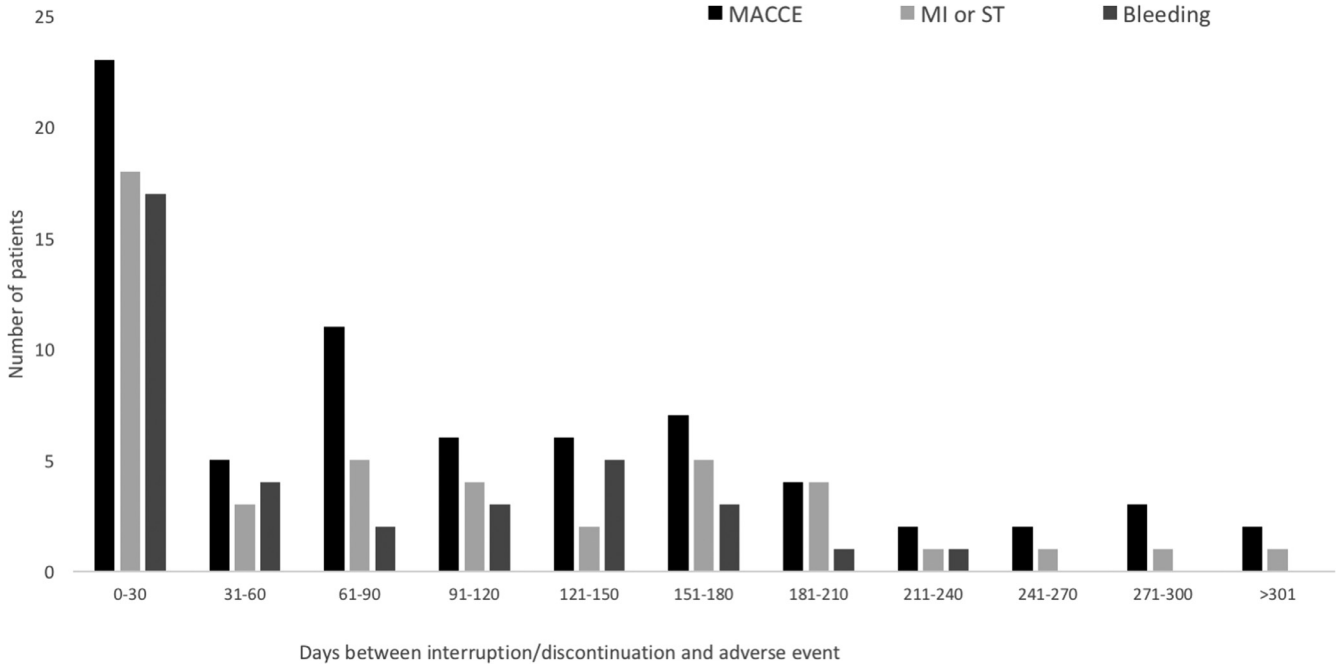

Figure 2. Time between interruption and adverse events. MACCE = major adverse cardiac and cerebrovascular events; MI = myocardial infarction; ST = stent thrombosis.

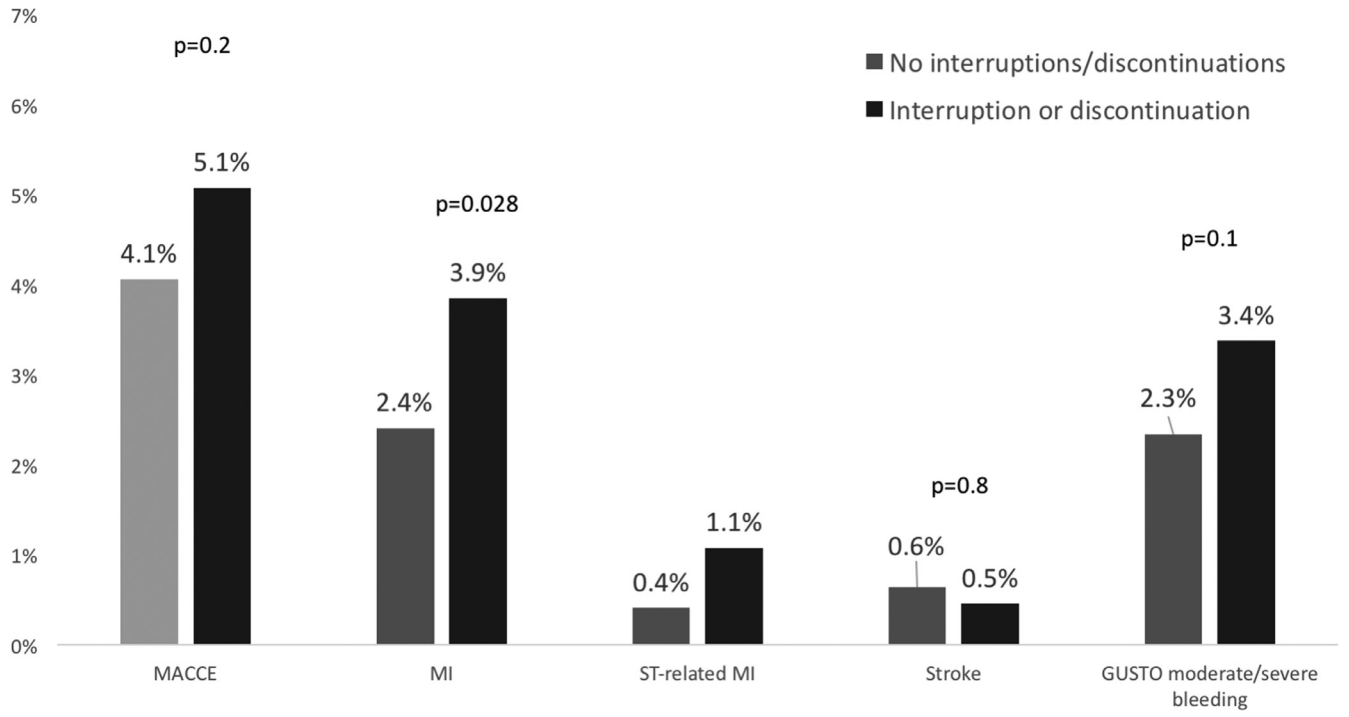

Figure 3. Incidence of adverse events in patients with vs. without interruptions of thienopyridine in sensitivity analysis population (n = 12,976). GUSTO = Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Arteries; MACCE = major adverse cardiac and cerebrovascular events; MI = myocardial infarction; ST = Stent thrombosis.

Table 5
Interaction of DAPT score and interruption status

Event	Interruption between 0-6 months (n = 1,173)	No interruption between 0-6 months (n = 21,829)	Hazard ratio [95% CI]	Log rank p value	p Value for interaction
Stent thrombosis or myocardial infarction after interruption					0.5
DAPT score <2	13 (2.4%)	224 (2.1%)	1.1 [0.6, 1.9]	0.750	
DAPT score ≥2	32 (5.4%)	428 (3.8%)	1.4 [0.97, 2.0]	0.069	
Major adverse cardiac and cerebrovascular events after interruption					0.6
DAPT score <2	28 (5.1%)	344 (3.2%)	1.5 [1.1, 2.3]	0.026	
DAPT score ≥2	43 (7.3%)	590 (5.3%)	1.4 [1.0, 1.9]	0.051	
GUSTO moderate/severe bleeding after interruption					0.7
DAPT score <2	19 (3.4%)	237 (2.2%)	1.5 [0.96, 2.4]	0.073	
DAPT score ≥2	17 (2.9%)	232 (2.1%)	1.4 [0.8, 2.2]	0.209	
Mortality after interruption					0.021
DAPT score <2	16 (2.9%)	113 (1.1%)	2.7 [1.6, 4.6]	<0.001	
DAPT score ≥2	10 (1.7%)	181 (1.6%)	1.0 [0.5, 1.9]	0.9	

reported in registries outside of clinical trials, ranging from 23.4% within a month of receiving a PCI with DES for treatment of an index MI in the PREMIER Registry,[15] to 28% in the first 3 months after an acute MI in the Acute Coronary Treatment and Intervention Outcomes Network Registry-Get With The Guidelines,[16] and 29.4% of patients with a DES placed in the previous 12 months in an analysis from the NCDR PINNACLE Registry.[17] The incidence of interruption of 5.1% at 6 months seen in our cohort is therefore at the lower end of reported data. Similar to previous studies,[9] we noted the highest risk for subsequent events was in the first month after interruption. We also noted that female subjects were more likely to have an interruption of therapy and were also more likely to suffer MACCE. In contrast to the PARIS Registry,[18] interruptions were also more common in subjects with diabetes mellitus versus those without in our cohort.

Several randomized trials have also addressed the issue of DAPT durations of <6 months compared with ≥6 months. Although these trials have suggested noninferiority of a shorter (3 or 6 months) duration of dual antiplatelet therapy after a PCI for stable ischemic heart disease[5] and low-complexity ACS,[7,8] our larger observational study does identify an increased risk of MACCE and MI after

interruptions of thienopyridine in that time frame. In contrast to these randomized trials, our study included a large, broadly representative subject population. As MACCE, MI and stent thrombosis are infrequent events in the first year after PCI, assessment of small differences based on duration of DAPT adherence requires large populations of unselected subjects at higher risk for these events that are less likely to be enrolled in studies randomizing to short-term DAPT. Nevertheless, results may be different in low risk populations as well as those at higher risk of bleeding, such as older age patients.[10,19] Unfortunately, our results do not indicate whether early interruption may be safer in subjects at lower risk for ischemic events or higher risk for bleeding events.

The nonadherence rate of 5.1% was observed in a carefully monitored trial with planned minimum duration of DAPT for 12 months before anticipated randomization. This rate may represent a conservative estimate relative to routine practice, especially given recent guideline recommendations supporting shorter durations and perhaps a lower threshold to interrupt therapy, in particular in patients with a higher risk of bleeding.[20–22] The incidence of MACCE or subsequent bleeding was similar regardless of the time to interruption over the first 6 months; although there were fewer interruptions in the first 30 days. As the majority of events occurred in the first 3 months after interruption, with the highest monthly incidence being in the first month, data-driven evaluation of the risk and benefit balance of thienopyridine interruption or discontinuation, as well as prompt resumption when indicated, is important.

There was no statistical interaction with DAPT score and interruption for ischemic or bleeding outcomes. In contrast, there was a significant interaction for all-cause mortality with interruption associated with higher mortality risk in subjects with DAPT score <2. It seems likely that this interaction is related to co-morbid factors in this group leading to initial interruption rather than subsequent effects of the DAPT nonadherence. The increased risk for bleeding after interruption is also of interest. It is likely that this represents the identification of a group at higher risk for bleeding, given that bleeding was a common reason for interruption. Although the underlying reason for the interruption is also a possible contributor to the early increase in the risk of MACCE, an increased risk of MI has also been described in randomized subjects during the first 3 months after randomized discontinuation of thienopyridine (months 12 to 15) in the DAPT study.[23]

This is an observational study, and despite adjusting for known and measured confounders, there are likely residual confounders that influence both the likelihood of interrupting/discontinuing thienopyridine after a PCI and having ischemic or bleeding events. As the events of interest in subjects who had an interruption or discontinued thienopyridine were only those that occurred after the interruption, those subjects had a shorter duration of follow-up than the subjects in the control group (no interruptions), who were followed for the full 12-month period. This would however bias our result toward the null. Interruptions of thienopyridine were first assessed at 6 months after PCI for the purposes of this analysis. We focused on interruption of thienopyridine and did not adjust for adherence to aspirin therapy. Finally, patients requiring oral anticoagulants were excluded from the primary DAPT study, likely contributing to a lower rate of interruption and limiting assessment of the subsequent effects in patients at highest bleeding risk.

In conclusion, in a large population planned to continue DAPT for 12 months after PCI, at least 5% of subjects had interruptions or had to discontinue thienopyridine in the first 6 months. This was associated with an increased incidence of MACCE, MI, and bleeding events subsequent to an interruption compared to subjects without interruptions.

Disclosures

Ada Stefanescu Schmidt: Nothing to Disclose

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Supplementary materials

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