



Validating Utility of Dual Antiplatelet Therapy Score in a Large Pooled Cohort From 3 Japanese Percutaneous Coronary Intervention Studies

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BACKGROUND: The dual antiplatelet therapy (DAPT) score was developed to estimate ischemic and bleeding risks from the DAPT study. However, few studies validated its utility externally. We sought to validate the utility of the DAPT score in the Japanese population.

METHODS: In a pooled cohort of 3 studies conducted in Japan (the CREDO-Kyoto [Coronary Revascularization Demonstrating Outcome Study in Kyoto] Registry Cohort-2, RESET [Randomized Evaluation of Sirolimus-Eluting Versus Everolimus-Eluting Stent Trial], and NEXT [NOBORI Biolimus-Eluting Versus XIENCE/PROMUS Everolimus-Eluting Stent Trial]), we compared risks for ischemic and bleeding events from 13 to 36 months after percutaneous coronary intervention among patients with a DAPT score ≥ 2 (high DS) and a DAPT score < 2 (low DS).

RESULTS: Among 12 223 patients receiving drug-eluting stents who were free from ischemic or bleeding events at 13 months after percutaneous coronary intervention, 3944 patients had high DS and 8279 had low DS. The cumulative incidence of primary ischemic end point (myocardial infarction/stent thrombosis) was significantly higher in high DS than in low DS (1.5% versus 0.9%, $P=0.002$), whereas the cumulative incidence of primary bleeding end point (GUSTO moderate/severe) tended to be lower in high DS than in low DS (2.1% versus 2.7%, $P=0.07$). The cumulative incidences of cardiac death, myocardial infarction, and stent thrombosis were also significantly higher in high DS than in low DS (2.0% versus 1.4%, $P=0.03$; 1.5% versus 0.8%, $P=0.002$; 0.7% versus 0.3%, $P<0.001$, respectively), whereas the cumulative incidences of noncardiac death and GUSTO severe bleeding were significantly lower in high DS than in low DS (2.4% versus 3.9%, $P<0.001$; 1.0% versus 1.6%, $P=0.03$, respectively).

CONCLUSIONS: In the current population, the DAPT score successfully stratified ischemic and bleeding risks, although the ischemic event rate was remarkably low even in high DS. Further studies would be warranted to evaluate the utility of prolonged DAPT guided by the DAPT score.

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Clinical Perspective

What Is New?

- We sought to validate the dual antiplatelet therapy (DAPT) score, which was developed to stratify the risks for ischemic and bleeding events with a single scoring system and to guide DAPT duration.
- In the pooled cohort of the current study, the incidence of primary ischemic end point was significantly higher in the high- than in the low-DAPT score, whereas the cumulative incidence of the primary bleeding end point tended to be lower in the high- than in the low-DAPT score.

What Are the Clinical Implications?

- In the current population composed of the 3 studies in Japan, the DAPT score successfully stratified the risks for both ischemic and bleeding events, although the ischemic event rate in the current population was remarkably low even in the high-DAPT score.
- Further studies would be warranted to evaluate the utility of prolonged DAPT guided by the DAPT score.

Dual antiplatelet therapy (DAPT) with aspirin and thienopyridine has been the standard care to prevent stent thrombosis (ST) in patients undergoing percutaneous coronary intervention (PCI) with drug-eluting stent (DES).^{1,2} In addition, extended DAPT is expected to reduce ischemic events such as myocardial infarction (MI) and possibly stroke in patients with advanced atherosclerotic after PCI.^{1,3,4} However, the optimal duration of DAPT after PCI with DES still remains a matter under debate. The DAPT study reported that prolonged DAPT reduced ischemic adverse events but increased bleeding events.³ It is challenging to identify who derives benefit or harm from prolonged DAPT because the predictive factors for ischemic and bleeding events often overlap.⁵ In the DAPT study, Yeh et al⁶ recently developed the DAPT score to estimate both the ischemic and bleeding risks with a single scoring system. The DAPT score successfully identified the 2 groups of patients internally within the DAPT study, in whom DAPT continuation beyond 1 year provided benefit of ischemic protection and in whom it caused harm from bleeding.^{3,6} However, the DAPT score has not been adequately validated externally outside the DAPT study. Furthermore, it is unclear whether prolonged DAPT guided by the DAPT score can reduce ischemic events in populations outside the DAPT study. Therefore, we sought to examine the utility of the DAPT score for stratifying the ischemic and bleeding risks and for guiding the duration of DAPT after DES implantation in a large pooled cohort from the 3 Japanese PCI studies.

METHODS

Study Population

We constructed a pooled database of 22 386 patients using the patient-level data from the 3 Japanese studies^{7–9} conducted by the same group of investigators, in which the status of antiplatelet therapy was consistently evaluated during the follow-up: the CREDO-Kyoto (Coronary Revascularization Demonstrating Outcome Study in Kyoto) PCI/CABG Registry Cohort-2 (Percutaneous Coronary Intervention/Coronary Artery Bypass Grafting) (N=15 939), the RESET trial (Randomized Evaluation of Sirolimus-Eluting Versus Everolimus-Eluting Stent) (N=3206), and the NEXT (NOBORI Biolimus-Eluting Versus XIENCE/PROMUS Everolimus-Eluting Stent Trial) (N=3241). The CREDO-Kyoto PCI/CABG Registry Cohort-2 is a multicenter observational registry that enrolled consecutive patients undergoing their first coronary revascularizations (January 2005–December 2007). RESET is a randomized controlled trial that compared sirolimus- with everolimus-eluting stent without any exclusion criteria (February–July 2010). NEXT is a randomized controlled trial that compared everolimus- with biolimus-eluting stent without any exclusion criteria (May–October 2011). The follow-up durations were 5 years in the CREDO-Kyoto PCI/CABG Registry Cohort-2 and 3 years in RESET and NEXT. For constructing the pooled database, the follow-up period was truncated at 3 years to standardize the follow-up duration. The study results and other details were previously reported^{7–9} and summarized in [Table 1 in the online-only Data Supplement](#).

The Kaplan-Meier curves for the clinical outcomes during the entire 3-year follow-up in the study group of 12 941 patients are presented in [Figure 1 in the online-only Data Supplement](#). The current study population consists of 12 223 patients who underwent successful PCI with DES, received DAPT at discharge, and were alive without MI, ST, or major bleeding events at 13 months after DES implantation (Figure 1). We evaluated the distribution of the DAPT score and compared the risks for ischemic and bleeding events beyond 13 months according to the 2 DAPT score categories (high DS versus low DS).

We also evaluated the association between DAPT status and ischemic and bleeding events beyond 13 months in the 2 DAPT score categories. Because the DAPT duration was determined by physicians and because the patient characteristics were different, we developed propensity score-matched cohorts of 5704 patients (N=1590 in high DS and N=4114 in low DS, evenly divided into on DAPT and off DAPT at 13 months) as the main set of exploratory analysis.

Baseline and Follow-Up Information and Definition of Clinical Events

In all 3 studies, most of the baseline and follow-up information was obtained from the hospital chart; for patients without a hospital visit, the follow-up information was collected by mail questionnaire or telephone to the patients and the referring physicians. MI was adjudicated by the definition of the ARTS (Arterial Revascularization Therapies Study)¹⁰ in the CREDO-Kyoto PCI/CABG Registry Cohort-2 and by the definition of Academic Research Consortium (ARC) consensus criteria¹¹ in RESET and NEXT. The definitions for the end points other than MI were identical across the 3 studies. Stent thrombosis was

defined according to the definition of the ARC.¹¹ Death was regarded as cardiac in origin unless obvious noncardiac causes could be identified. Stroke during follow-up was defined as ischemic or hemorrhagic stroke requiring hospitalization with symptoms lasting >24 hours. Bleeding was defined according to the GUSTO classification (Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries).¹² The clinical events were adjudicated by independent clinical event committees. Each study protocol was approved by the institutional review boards in all the participating centers. In the CREDO-Kyoto PCI/CABG Registry Cohort-2, written informed consent from the patients was waived because of its retrospective enrollment, although those who refused participation when contacted for follow-up were excluded. In RESET and NEXT, written informed consents were obtained from all the study subjects.

DAPT Score Calculation

The details of the DAPT score calculation were reported previously.⁶ Briefly, the score, ranging from -2 to 10, assigned points as follows: 0 point for patients <65 years of age; -1 point for 65 to <75 years of age; -2 point for patients ≥75 years of age; 2 points for vein graft stenting and history of congestive heart failure or left ventricular ejection fraction (LVEF) <30%; and 1 point for current cigarette smoker or within a year, diabetes mellitus, MI at presentation, stent diameter <3 mm, prior PCI or MI, and paclitaxel-eluting stent. The study patients were separated into the 2 categories previously reported⁶: DAPT score ≥2 (high DS) and DAPT score <2 (low DS). As an exploratory subgroup analysis, the low-DS group was further divided into DAPT score=1 (middle DS) and DAPT score <1 (very low DS). In the current data set, the data on LVEF was lacking in a significant proportion of patients (N=1895, 15.5%). To avoid exclusion of those patients

without LVEF data, we regarded those patients as having LVEF ≥30% when they did not have a history of congestive heart failure. Calculation of the DAPT score was performed by 2 physicians (Y.Y. and H.W.) in a fashion blinded to the clinical outcomes.

Antithrombotic Therapy

Procedural anticoagulation was achieved with unfractionated heparin following the local site protocols. The recommended antiplatelet regimen included aspirin (≥81 mg daily) indefinitely and thienopyridines (75 mg clopidogrel or 200 mg ticlopidine daily) for ≥3 months in RESET and NEXT. There was no specific protocol-recommended antiplatelet therapy in the CREDO-Kyoto PCI/CABG Registry Cohort-2 because of its retrospective observational study design. The actual duration of DAPT was left to the discretion of each attending physician in all the studies. The status of antiplatelet therapy was evaluated throughout the follow-up period. Discontinuation of aspirin or thienopyridine was defined to be persistent when withdrawn for ≥2 months.¹³ Discontinuation of DAPT was defined as persistent discontinuation of either aspirin or thienopyridine.

Outcome Measures

The primary ischemic end point was defined as a composite of MI (defined by the ARTS in the CREDO-Kyoto PCI/CABG Registry Cohort-2 and by the ARC criteria in RESET and NEXT) and definite/probable ST (defined by the ARC criteria).^{10,11} The primary bleeding end point was defined as moderate or severe bleeding by the GUSTO classification.¹² The secondary end point included the individual components of the primary end points, all-cause death, cardiac death, noncardiac death, and stroke. The detailed definitions of these end points are described in this report and presented previously.⁷⁻⁹

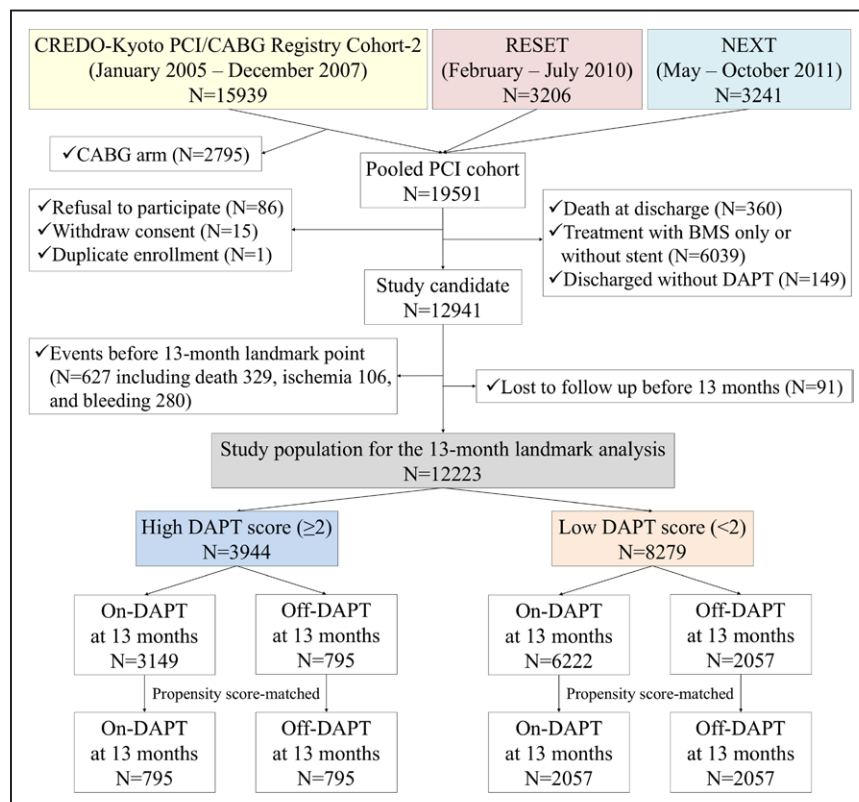


Figure 1. Study flow chart.

We constructed a pooled database of 22 386 patients using patient-level data from the 3 Japanese studies conducted by the same group of investigators: the CREDO-Kyoto PCI/CABG Registry Cohort-2, RESET, and NEXT. A total of 12 223 patients were included in this pooled analysis. BMS indicates bare-metal stent; CABG, coronary artery bypass grafting; CREDO-Kyoto, Coronary Revascularization Demonstrating Outcome Study in Kyoto; DAPT, dual antiplatelet therapy; NEXT, NOBORI Biolimus-Eluting Versus XIENCE/PROMUS Everolimus-Eluting Stent Trial; PCI, percutaneous coronary intervention; and RESET, Randomized Evaluation of Sirolimus-Eluting Versus Everolimus-Eluting Stent Trial.

Statistical Analysis

Categorical variables were presented as counts and percentages and were compared by the χ^2 test or Fisher exact test. Continuous variables were presented as mean $\pm$ SD or median with interquartile range. Continuous variables were compared using the Student *t* test or Wilcoxon rank-sum test depending on their distributions. Cumulative incidences of events were estimated by the Kaplan-Meier method, and the differences were assessed by the log-rank test. To evaluate clinical outcomes beyond 1 year, we conducted a so-called landmark analysis at 13 months, taking a window period of 1 month because the patients in the DAPT study and those in our previous study were allocated in similar timelines.^{3,14}

As an exploratory analysis, we sought to evaluate the association between longer DAPT and clinical outcomes in patients with high DS and low DS, respectively. We divided the patient population into 2 groups according to the DAPT status at 13 months (on DAPT, N=3149 in high DS and N=6222 in low DS; off DAPT, N=795 in high DS and N=2057 in low DS). We used the logistic regression model to develop a propensity score for the choice of DAPT status at the landmark point in each DAPT score category with 23 variables relevant to the DAPT choice listed in [Tables II and III in the online-only Data Supplement](#). Missing data were considered as negative values for binary covariates, because the numbers of missing data were negligibly small (maximum of 89 out of 12223 patients for the variable of hemoglobin <11 g/dL). The propensity score was calculated by summing up all the coefficients multiplied by corresponding variables. To create the propensity score-matched cohort, the patients on DAPT at 13 months were matched to those without DAPT at 13 months using the 1:1 greedy matching technique.¹⁵ Then we calculated

the cumulative incidences of the primary end points and their individual components by the Kaplan-Meier method, and the differences were assessed by the log-rank test.

We conducted an additional sensitivity analysis using the Cox proportional hazard model with DAPT status as a time-updated covariate. We estimated the risks of on DAPT relative to off DAPT for the primary end points by the multivariable Cox proportional hazard model by DAPT status at 13 months as on versus off approach (model 1), and by the multivariable Cox proportional hazard model with DAPT status beyond 13 months as a time-updated covariate (model 2), using the same clinically relevant variables listed in [Tables II and III in the online-only Data Supplement](#). The detailed methods were described in the [Methods and Results in the online-only Data Supplement](#).

The statistical analyses were conducted by 2 physicians (Y.Y. and H.W.) and a statistician (T.M.). The propensity score was calculated with SAS 9.4 (SAS Institute Inc.). The multivariable Cox proportional hazard model with stratification variable and time-updated covariate was performed with SPSS version 19 (IBM Corp.). All the other analyses were performed with JMP version 13.1 (SAS Institute Inc.). All the reported *P* values were 2-sided, and *P* values <0.05 were considered statistically significant.

RESULTS

Baseline Characteristics: High- Versus Low-DAPT Score Categories

Among the 12223 study patients, 3944 (32%) had high DS and 8279 (68%) had low DS (Figure 2). The

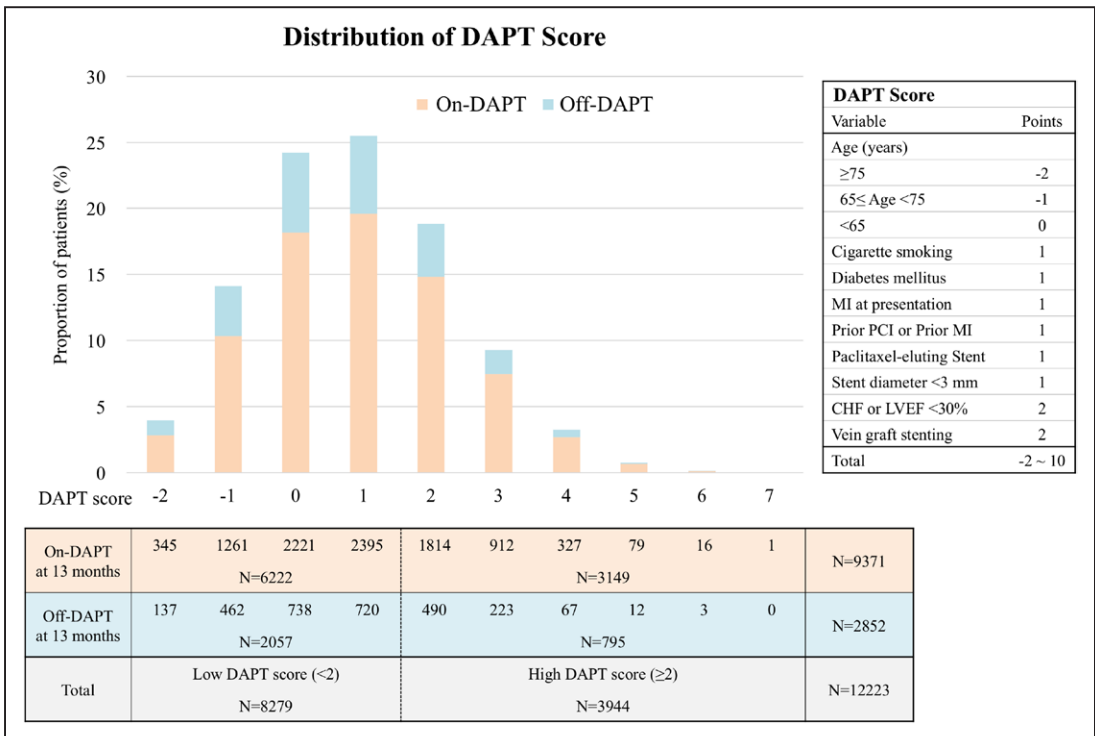


Figure 2. Distribution of DAPT score.

The bar chart represents the proportion of the patients in each DAPT score. In each DAPT score category, the patients were divided into 2 groups according to the DAPT status at the 13-month landmark point (on DAPT and off DAPT). CHF indicates congestive heart failure; DAPT, dual antiplatelet therapy; LVEF, left ventricular ejection fraction; MI, myocardial infarction; and PCI, percutaneous coronary intervention.

Table 1. Baseline Characteristics: High- Versus Low-DAPT Score Categories

	High-DAPT score (N=3944)		Low-DAPT score (N=8279)		P Value
Clinical characteristics					
Age	62.0±9.1		71.6±8.9		<0.001
Age ≥75, y	258	(6.5%)	3440	(41.6%)	<0.001
Male	3259	(83%)	5878	(71%)	<0.001
Body mass index	24.6±3.7		23.8±3.3		<0.001
Clinical presentation					
Acute myocardial infarction	838	(21%)	752	(9.1%)	<0.001
Unstable angina pectoris	269	(6.8%)	839	(10%)	<0.001
Stable coronary artery disease	2837	(72%)	6688	(81%)	<0.001
Hypertension	3196	(81%)	6797	(82%)	0.16
Diabetes mellitus	2644	(67%)	2587	(31%)	<0.001
Diabetes on insulin	683	(17%)	523	(6.3%)	<0.001
Current smoking	1875	(48%)	1076	(13%)	<0.001
History of congestive heart failure	591	(15%)	152	(1.8%)	<0.001
Multivessel disease	2434	(62%)	4381	(53%)	<0.001
LVEF	55.5±13.8		61.8±11.0		<0.001
LVEF <30%	204	(5.2%)	34	(0.4%)	<0.001
Prior myocardial infarction	1281	(32%)	1239	(15%)	<0.001
Prior PCI	1318	(33%)	1672	(20%)	<0.001
Prior stroke	379	(9.6%)	917	(11%)	0.01
Peripheral vascular disease	223	(5.7%)	577	(7.0%)	0.005
HD or eGFR <30	323	(8.2%)	552	(6.3%)	<0.001
eGFR <30 non-HD	99	(2.5%)	229	(2.8%)	0.41
HD	224	(5.7%)	293	(3.5%)	<0.001
Atrial fibrillation	221	(5.6%)	609	(7.4%)	<0.001
COPD	96	(2.4%)	228	(2.8%)	0.30
Liver cirrhosis	53	(1.3%)	122	(1.5%)	0.57
Malignancy	180	(4.6%)	716	(8.7%)	<0.001
Hemoglobin <11.0 g/dL	385	(9.8%)	916	(11%)	0.03
Platelet <10 ⁵ /μL	49	(1.3%)	107	(1.3%)	0.81
Procedural characteristics					
Number of target lesions	1.56±0.81		1.39±0.68		<0.001
Target of unprotected LMCA	129	(3.3%)	278	(3.4%)	0.80
Target of chronic total occlusion	591	(15%)	750	(9.1%)	<0.001
Target of bifurcation lesion	1363	(35%)	2679	(32%)	0.02
Side-branch stenting	193	(4.9%)	316	(3.8%)	0.006
Total number of stents	2.09±1.30		1.76±1.11		<0.001
Total stent length	45.5±31.4		37.4±26.7		<0.001
Total stent length >28 mm	2319	(59%)	3807	(46%)	<0.001
Minimum stent diameter	2.72±0.35		2.90±0.38		<0.001
Minimum stent diameter <3 mm	2736	(69%)	3506	(42%)	<0.001
Vein graft stenting	24	(0.6%)	5	(0.1%)	<0.001
1st generation drug eluting stent	2451	(62%)	5179	(63%)	0.66
Sirolimus-eluting stent	2226	(56%)	5018	(61%)	<0.001
Paclitaxel-eluting stent	327	(8.3%)	237	(2.9%)	<0.001

(Continued)

Table 1. Continued

	High-DAPT score (N=3944)		Low-DAPT score (N=8279)		P Value
2nd generation drug-eluting stent	1517	(38%)	3119	(38%)	0.40
Everolimus-eluting stent	1005	(26%)	2037	(25%)	0.29
Biolimus-eluting stent	512	(13%)	1087	(13%)	0.82
Zotarolimus-eluting stent	4	(0.1%)	8	(0.1%)	0.94
Bare-metal stent	487	(12%)	553	(6.7%)	<0.001
Discharge medication					
Ticlopidine	2039	(52%)	4253	(51%)	0.73
Clopidogrel	1896	(48%)	3993	(48%)	0.87
Cilostazol	544	(14%)	831	(10%)	<0.001
Statins	2809	(71%)	5325	(64%)	<0.001
β-blockers	1593	(40%)	2471	(30%)	<0.001
ACE-I/ARB	2689	(68%)	4608	(56%)	<0.001
Warfarin	355	(9.0%)	585	(7.1%)	<0.001
Study					
CREDO-Kyoto Registry Cohort-2	1974	(50%)	4232	(51%)	0.47
RESET	984	(25%)	1991	(24%)	
NEXT	986	(25%)	2056	(25%)	

ACE-I indicates angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; COPD, chronic obstructive pulmonary disease; CREDO-Kyoto, Coronary Revascularization Demonstrating Outcome Study in Kyoto; DAPT, dual antiplatelet therapy; eGFR, estimated glomerular filtration rate; HD, hemodialysis; LMCA, left main coronary artery; LVEF, left ventricular ejection fraction; NEXT, NOBORI Biolimus-Eluting Versus XIENCE/PROMUS Everolimus-Eluting Stent Trial; PCI, percutaneous coronary intervention; RESET, Randomized Evaluation of Sirolimus-Eluting Versus Everolimus-Eluting Stent Trial; and SD, standard deviation. Categorical variables are presented as n (%), and continuous variables are presented as mean±SD.

high-DS group had a significantly higher proportion of patients with acute MI at presentation, diabetes mellitus, current smoking, history of congestive heart failure, LVEF <30%, prior MI, and hemodialysis than the low-DS group, whereas the low-DS group had a significantly higher proportion of patients with advanced age, female sex, prior stroke, peripheral artery disease, atrial fibrillation, malignancy, and anemia than the high-DS group. Regarding the procedure characteristics, the high-DS group generally had more complex features, such as a higher proportion of multivessel disease and a longer stent length than the low-DS group. Medications such as statins, β-blockers, and angiotensin-converting enzyme inhibitors or angiotensin receptor blockers were more often prescribed in the high-DS than in the low-DS group (Table 1).

Clinical Outcomes by the 13-Month Landmark Analysis: High- Versus Low-DAPT Score Categories

The cumulative 3-year incidence of the primary ischemic end point beyond 13 months after PCI was significantly higher in the high-DS than in the low-DS group (1.5% versus 0.9%, log-rank $P=0.002$), although the event rate was remarkably low even in the high-DS group (Figure 3A and Table 2). The cumulative 3-year incidence of the primary bleeding end point beyond 13 months after

PCI tended to be lower in the high-DS than in the low-DS group without a statistically significant difference (2.1% versus 2.7%, log-rank $P=0.07$) (Figure 3B and Table 2).

Regarding the secondary outcome measures, the high-DS group was associated with significantly higher cumulative 3-year incidences of cardiac death, MI, and definite/probable ST than the low-DS group (2.0% versus 1.4%, log-rank $P=0.03$; 1.5% versus 0.8%, log-rank $P=0.002$; 0.7% versus 0.3%, log-rank $P<0.001$, respectively), whereas the low-DS group was associated with significantly higher cumulative 3-year incidences of non-cardiac death and GUSTO severe bleeding than the high-DS group (2.4% versus 3.9%, log-rank $P<0.001$; 1.0% versus 1.6%, log-rank $P=0.03$, respectively) (Table 2).

In the additional analysis stratified by the 3 DAPT score categories (high DS, middle DS, and very low DS), the Kaplan-Meier curves diverged in order of the DAPT score categories for both the primary ischemic end point and the primary bleeding end point (Figure II in the online-only Data Supplement).

Baseline Characteristics and Clinical Outcomes in Propensity Score-Matched Cohort According to DAPT Status at 13 Months

In both the high-DS (N=3944) and low-DS (N=8279) groups, large proportions of patients (3149 [80%] and

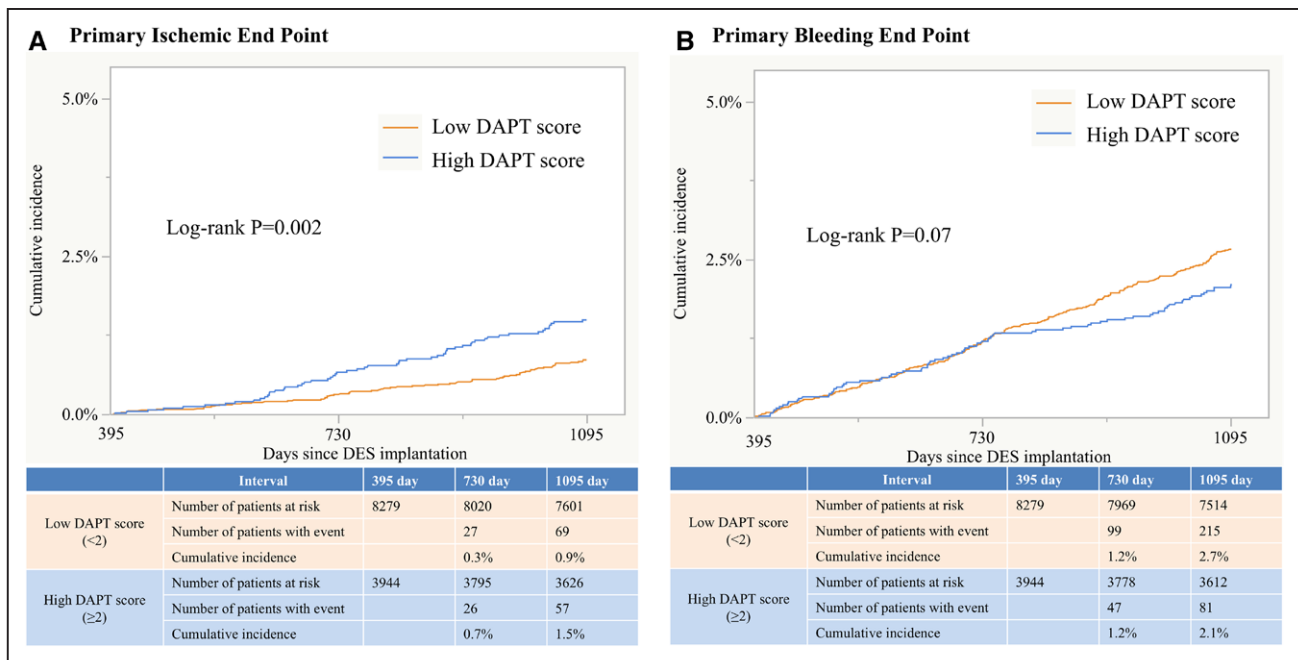


Figure 3. The cumulative 3-year incidences of the primary ischemic end point.

The cumulative 3-year incidences of the primary ischemic end point (A) and the primary bleeding end point (B) by the 13-month landmark analysis: high- versus low-DAPT score categories. The cumulative 3-year incidence of the primary ischemic end point (a composite of myocardial infarction or definite/probable stent thrombosis) was significantly higher in the patients with a high-DAPT score than in those with a low-DAPT score, whereas that of the primary bleeding end point (GUSTO moderate/severe bleeding) tended to be lower in those with a high-DAPT score than in those with a low-DAPT score without statistically significant difference. DAPT indicates dual antiplatelet therapy; DES, drug-eluting stent; and GUSTO, Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries.

6222 [75%], respectively) continued DAPT (on-DAPT group) at the 13-month landmark point (Figure 2). Compared with the off-DAPT group ($N=795$ and $N=2057$, respectively), the on-DAPT group included more patients with diabetes mellitus, prior MI, prior stroke, hemodialysis, and target of left main coronary artery lesion but fewer patients with acute MI at presentation and liver cirrhosis. The stent types and medications were also significantly different between the on- and off-DAPT groups, reflecting the higher prevalence of newer studies such as RESET and NEXT in the on-DAPT group (Tables II and III in the online-only Data Supplement).

The baseline characteristics of the on- and off-DAPT groups in the propensity score-matched cohorts in each score category were much more comparable than those in the entire cohort (Tables IV and V in the online-only Data Supplement).

In the propensity score-matched high-DS cohort, the cumulative 3-year incidence of the primary ischemic end point tended to be lower in the on- than off-DAPT group (0.9% versus 1.9%, log-rank $P=0.10$), whereas that of the primary bleeding end point was not different between the on- and off-DAPT groups (1.9% versus 2.2%, log-rank $P=0.76$) (Figure 4 and Table 3).

Conversely, in the propensity score-matched low-DS cohort, the cumulative 3-year incidence of the primary

bleeding end point tended to be higher in the on- than in the off-DAPT group (3.2% versus 2.3%, log-rank $P=0.08$), whereas that of the primary ischemic end point was not different between the on- and off-DAPT groups (0.8% versus 1.0%, log-rank $P=0.51$) (Figure 5 and Table 4).

In the sensitivity analyses using multivariable Cox proportional hazard models, none of the hazard ratios or interactions was significant, as in the propensity score-matched analyses. The detailed results are shown in Table VI in the online-only Data Supplement.

DISCUSSION

The main findings of the current study were as follows: (1) the DAPT score successfully stratified the ischemic and bleeding risks beyond 1 year after PCI with DES in the Japanese population; (2) the event rate of MI and ST in the present study was remarkably low even in patients with high DS; (3) in the propensity score-matched cohort, the on-DAPT group at 13 months compared with the off-DAPT group tended to be at a lower risk for ischemic events in high DS and at a higher risk for bleeding events in low DS, although the differences were not statistically significant.

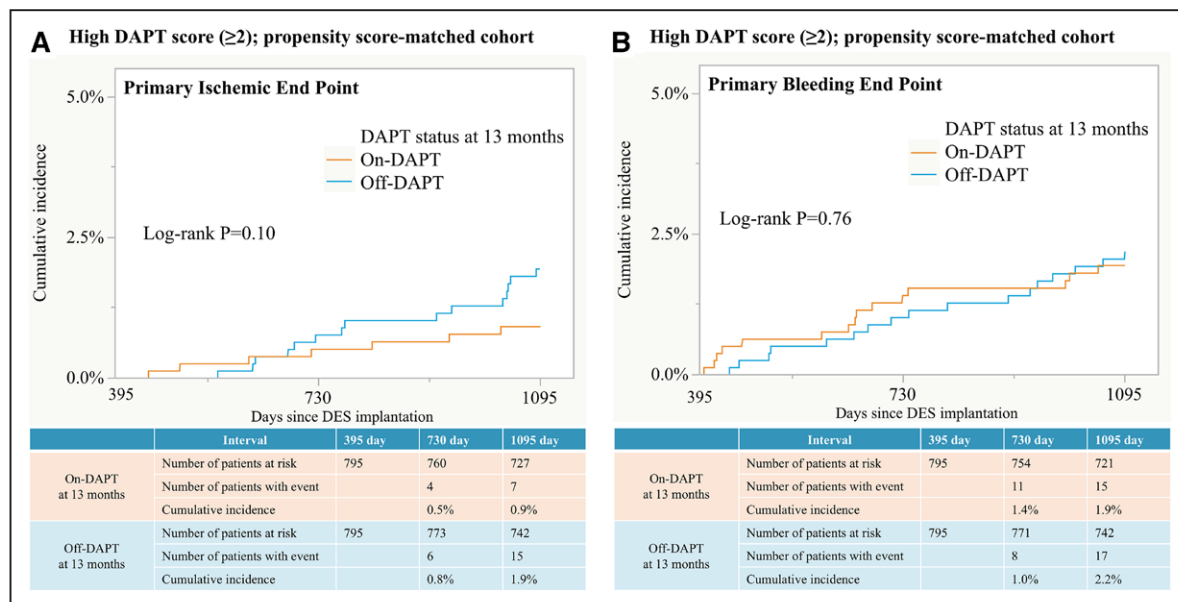
Table 2. Clinical Outcomes at 3 Years by the 13-Month Landmark Analysis: High- Versus Low-DAPT Score Categories

	High-DAPT score		Low-DAPT score		Log-Rank <i>P</i> Value
	(N=3944)		(N=8279)		
	Number of Patients With Event				
	(Cumulative incidence)				
Ischemic event					
Primary ischemic end point (MI+definite/probable ST)	57	(1.5%)	69	(0.9%)	0.002
MI	56	(1.5%)	67	(0.8%)	0.002
Definite/probable ST	28	(0.7%)	21	(0.3%)	<0.001
Definite ST	21	(0.6%)	14	(0.2%)	<0.001
Bleeding event					
Primary bleeding end point (GUSTO moderate/severe)	81	(2.1%)	215	(2.7%)	0.07
GUSTO moderate	43	(1.1%)	93	(1.2%)	0.87
GUSTO severe	40	(1.0%)	124	(1.6%)	0.03
Stroke					
Ischemic/hemorrhagic	68	(1.8%)	166	(2.1%)	0.29
Ischemic	49	(1.3%)	116	(1.5%)	0.48
Hemorrhagic	19	(0.5%)	51	(0.6%)	0.36
Death					
All-cause death	168	(4.3%)	430	(5.2%)	0.03
Cardiac death	76	(2.0%)	116	(1.4%)	0.03
Noncardiac death	92	(2.4%)	314	(3.9%)	<0.001

DAPT indicates dual antiplatelet therapy; GUSTO, Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries; MI, myocardial infarction; and ST, stent thrombosis. Cumulative incidences were estimated by the Kaplan-Meier method.

In line with the DAPT study and its external validation cohort (PROTECT trial [Patient Related Outcomes With Endeavor Versus Cypher Stenting]), the DAPT score

successfully stratified the long-term risk for the ischemic events beyond 1 year after PCI with DES in this additional external validation cohort of the Japanese population.^{6,16}

**Figure 4.** The cumulative 3-year incidences of the primary end points in the propensity score-matched cohort of the high-DAPT score group.

A, The cumulative 3-year incidence of the ischemic end point. **B**, The cumulative 3-year incidence of the bleeding end point. In the high-DAPT score group, the cumulative incidence of primary ischemic end point tended to be lower in the on- than in the off-DAPT group, whereas that of primary bleeding end point was not different between the on- and off-DAPT groups. DAPT indicates dual antiplatelet therapy; and DES, drug-eluting stent.

Table 3. Clinical Outcomes at 3 Years by the 13-Month Landmark Analysis in the Propensity Score-Matched Cohort: On- Versus Off-DAPT Group at the 13-Month Landmark Point

DAPT score ≥2 (propensity score-matched)	On DAPT at 13 Months (N=795)		Off DAPT at 13 Months (N=795)		Log-Rank P Value
	Number of Patients With Event (Cumulative Incidence)				
Ischemic event					
Primary ischemic end point (MI+definite/probable ST)	7	(0.9%)	15	(1.9%)	0.10
MI	7	(0.9%)	15	(1.9%)	0.09
Definite/probable ST	4	(0.5%)	8	(1.0%)	0.26
Definite ST	3	(0.4%)	8	(1.0%)	0.13
Bleeding event					
Primary bleeding end point (GUSTO moderate/severe)	15	(1.9%)	17	(2.2%)	0.76
GUSTO moderate	8	(1.1%)	12	(1.6%)	0.39
GUSTO Severe	7	(0.9%)	6	(0.8%)	0.76

DAPT indicates dual antiplatelet therapy; GUSTO, Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries; MI, myocardial infarction; and ST, stent thrombosis. Cumulative incidences were estimated by the Kaplan-Meier method.

It would be important to note that the proportion of patients with high DS and their ischemic event rate from 1 year through 30 months were lower in the present study than in the DAPT study (32% versus 51% and 0.7% versus 3.0%, respectively).⁶ Therefore, the absolute risk of ischemic events in patients with high or low DS could be different according to the ethnic and/or geographic differences. As to bleeding events, the DAPT score could discriminate the long-term bleeding risk internally in the DAPT study but not in the external validation cohort (the PROTECT trial). The discrepancy between the DAPT study and the PROTECT trial might be at least partly explained by the difference in the rate of bleeding events from 1 year through 30 months between the 2 studies (1.8% in the DAPT study, and 0.4% in high DS and 0.5% in low DS in the PROTECT trial).⁶ Indeed, in the present study, there was a trend toward a higher bleeding risk in patients with low DS, in which the rate of bleeding

events from 1 year through 30 months using the same end point definition was similar to that in the DAPT study (1.8% versus 1.8%).⁶ Therefore, the DAPT score would also be applicable in the Japanese population for assessing both ischemic and bleeding risks.

Although the DAPT study demonstrated remarkable reduction in the ischemic events by the prolonged DAPT in the high-DS group, the ischemic risk of on DAPT in the high-DS group tended to be lower than that of off DAPT but was not statistically significant in the present study. This discrepancy might be at least partly explained by the difference in the rates of ischemic events from 1 year through 30 months in the high-DS groups between the 2 studies (2.7% versus 5.7% for continued thienopyridine versus placebo in the DAPT study; 1.1% versus 1.0% for on- versus off-DAPT in the present study).⁶ As shown in the results, the overall ischemic event rate in the present study

Table 4. Clinical Outcomes at 3 Years by the 13-Month Landmark Analysis in the Propensity Score-Matched Cohort: On- Versus Off-DAPT Group at the 13-Month Landmark Point

DAPT score <2 (propensity score-matched)	On DAPT at 13 Months (N=2057)		Off DAPT at 13 Months (N=2057)		Log-Rank P Value
	Number of Patients With Event (Cumulative Incidence)				
Ischemic event					
Primary ischemic end point (MI+definite/probable ST)	16	(0.8%)	20	(1.0%)	0.51
MI	16	(0.8%)	19	(1.0%)	0.61
Definite/probable ST	6	(0.3%)	8	(0.4%)	0.59
Definite ST	2	(0.1%)	6	(0.3%)	0.15
Bleeding event					
Primary bleeding end point (GUSTO moderate/severe)	63	(3.2%)	45	(2.3%)	0.08
GUSTO moderate	29	(1.5%)	17	(0.9%)	0.07
GUSTO severe	35	(1.8%)	28	(1.4%)	0.37

DAPT indicates dual antiplatelet therapy; GUSTO, Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries; MI, myocardial infarction; and ST, stent thrombosis. Cumulative incidences were estimated by the Kaplan-Meier method.

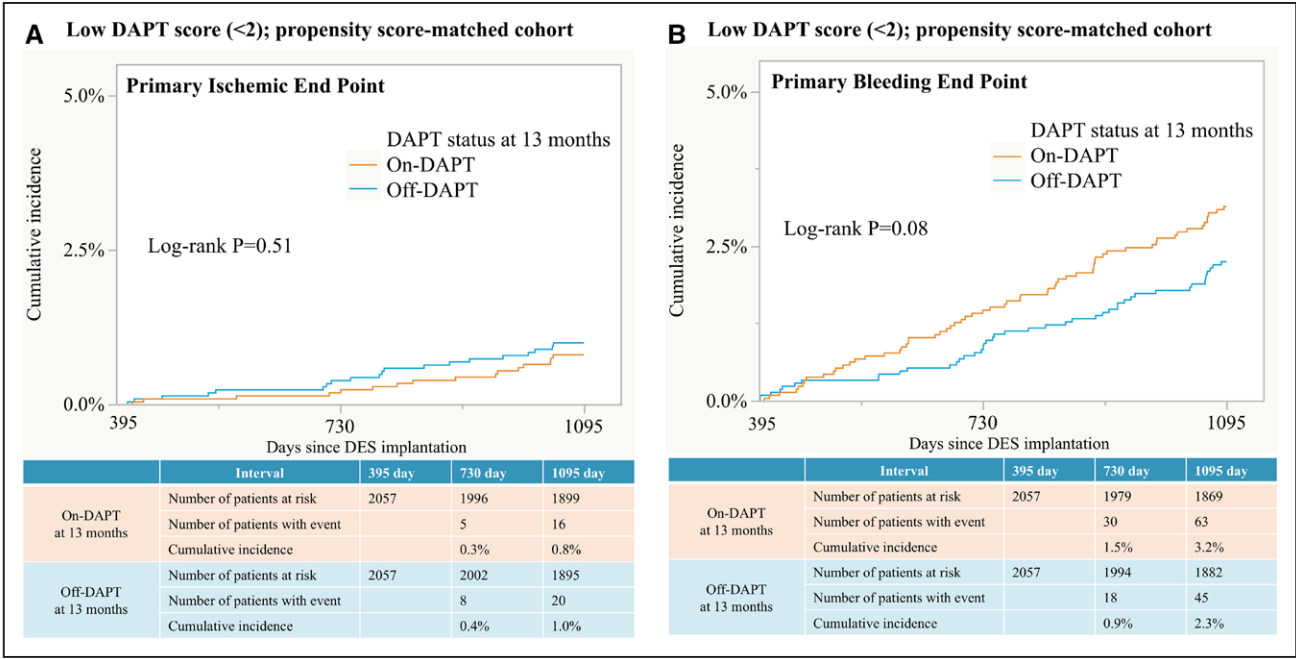


Figure 5. The cumulative 3-year incidences of the primary end points in the propensity score-matched cohort of the low-DAPT score group. **A**, The cumulative 3-year incidence of the ischemic end point. **B**, The cumulative 3-year incidence of the bleeding end point. In the low-DAPT score group, the cumulative incidence of primary bleeding end point tended to be higher in the on- than in the off-DAPT group, whereas that of primary ischemic end point was not different between the on- and off-DAPT groups. DAPT indicates dual antiplatelet therapy; and DES, drug-eluting stent.

was lower than the bleeding event rate. In contrast, in the DAPT study as well as another study of prolonged DAPT, PEGASUS-TIMI 54 (Patients With Prior Heart Attack Using Ticagrelor Compared to Placebo on a Background of Aspirin-Thrombolysis in Myocardial Infarction 54),⁴ the overall ischemic event rates tended to be higher than the bleeding event rates. The lower risks for ischemic events in the present study might have influenced the association between longer DAPT and clinical outcomes. Another possible reason for the discrepancy between the DAPT study and the current study could be the difference in the clinical presentation of the patients. There were fewer patients with acute myocardial infarction in the current study (13%) than in the DAPT study (26%).³ Taking these factors into consideration, the efficacy of prolonged DAPT for ischemic protection is still debatable.

Bleeding risks were also not significantly different between the on- and off-DAPT groups in the present study. However, in the low-DS group in the current study, the on-DAPT group compared with the off-DAPT group tended to be at a higher risk for the primary bleeding end point. In the DAPT study, prolonged DAPT compared with shorter DAPT was associated with a significantly higher bleeding risk and a trend toward increased mortality. In the ADAPT-DES study (Assessment of Dual Antiplatelet Therapy With Drug-Eluting Stents), bleeding after discharge after PCI was strongly

associated with 2-year mortality (hazard ratio [HR], 5.03; 95% confidence interval [CI], 3.29–7.66), with an effect size greater than that of myocardial infarction after discharge (HR, 1.92; 95% CI, 1.18–3.12).¹⁷ In the present study, the patients with low DS constituted a large proportion of the entire cohort. It might be more important to avoid bleeding events than to prevent ischemic events for a population at low ischemic risk and high bleeding risk such as the Japanese.

Limitations

The current study has several important limitations. First, all the studies involved in the current analyses did not randomize the duration of DAPT. Therefore, the results for the DAPT duration in this study are hypothesis generating because of its observational study design and lack of adequate power. The analysis does not really compare on versus off treatment during the follow-up period. Furthermore, >70% of patients continued DAPT independent of the DAPT score groups. It is likely that those who came off therapy were suspected to have higher bleeding risk, lower ischemic risk, or both. The result of this might be to bias any effect of DAPT continuation to the null. Therefore, the current analyses could not make any definitive conclusions about the effect of different DAPT durations on clinical outcomes in the 2 DAPT score categories. Second, the population of the current

pooled analyses consisted of the patients from a registry (the CREDO-Kyoto PCI/CABG Registry Cohort-2) and randomized controlled trials (RESET and NEXT), which were conducted in different time periods and contexts. Third, the definitions for MI were different between the CREDO-Kyoto PCI/CABG Registry Cohort-2 and the 2 randomized controlled trials (RESET and NEXT). MI was adjudicated by the definition of ARTS in the CREDO-Kyoto PCI/CABG Registry Cohort-2 and by the definition of ARC consensus criteria in RESET and NEXT. However, both the ARTS and ARC definitions adopted the same criteria for spontaneous MI (biomarker elevation above upper limit of normal). The present study evaluated clinical outcomes between 13 and 36 months after PCI, when the vast majority of adjudicated MI was not procedure-related MI but spontaneous MI. Therefore, the difference in definitions of MI would not have affected the results in the present study. Fourth, a significant proportion of patients in this study received ticlopidine as thienopyridines, which is different from the current usual care. The results of this study might be less generalizable because of this difference in thienopyridine use. Fifth, risk adjustment by continuous variables theoretically improves the power to detect differences compared with that by dichotomized variables. However, we have consistently dichotomized the continuous variables in our previous reports. Finally, as discussed, the overall ischemic event rate in the present study was remarkably lower than that in the DAPT study and was $\approx 25\%$ of that of the DAPT study. The difference in potential risk for ischemic events might have influenced the association between DAPT and ischemic events. Indeed, in the current 3 physician-directed studies, patients were not fully monitored, and the collection of clinical events was based on self-report by the site investigators. We could not exclude the possibility of underreporting clinical events. However, low rates of ischemic events have been reported consistently in the fully monitored company-directed postmarket surveillance registries of DES in Japan.^{18,19}

Conclusions

The DAPT score successfully stratified the ischemic and bleeding risks beyond 13 months after PCI with DES in the Japanese population, although the ischemic event rate was remarkably low even in the high-DAPT score group. Further studies would be warranted to evaluate the utility of prolonged DAPT guided by the DAPT score.

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DISCLOSURES

Dr Kimura is an advisory board member of Terumo Japan and Abbott Vascular and reports research grants from Abbott Vascular. The other authors report no conflicts.

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FOOTNOTES

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Validating Utility of Dual Antiplatelet Therapy Score in a Large Pooled Cohort From 3 Japanese Percutaneous Coronary Intervention Studies
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Supplemental Material

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Supplemental Methods and Results

We conducted an additional sensitivity analysis using the Cox proportional hazard model with a time-updated covariate. We estimated the risks of on-DAPT relative to off-DAPT for the primary end points by the multivariable Cox proportional hazard model with DAPT status at 13 months as on versus off (model 1), and by the multivariable Cox proportional hazard model with DAPT status beyond 13 months as a time-updated covariate (model 2), using the same clinically relevant variables listed in Supplemental Table 2 and 3. The patients who discontinued DAPT persistently before or after the 13-month landmark point were regarded as off-DAPT, while those without persistent discontinuation or only temporary discontinuation for less than two months were regarded as on-DAPT.^{1,2} In the model 2, once DAPT status changed from on-DAPT to off-DAPT, the covariate of DAPT status was regarded as off-DAPT until the censor or the end of follow-up. The study code and the center code were incorporated as stratification variables. The proportional hazard assumptions were verified for each variable by the plot of log (time) versus log [-log (survival)]. Continuous variables were dichotomized by clinically meaningful reference values or median values in line with our previous reports.³⁻⁵ The risks of on-DAPT relative to off-DAPT for the primary end points were expressed as hazard ratios (HR) and their 95% confidence intervals (CI).

For decision of DAPT duration by each attending physician, DAPT would have been mostly discontinued when bleeding events occurred. Therefore, for the evaluation of the risk for ischemic end point in the model 2, we also assessed the risk for the ischemic end point which was censored when a bleeding end point occurred before the ischemic end point. The statistical methods other than the censoring were the same as described above.

The results are shown in Supplemental Table 6. In the high DAPT score category, the risks of on-DAPT relative to off-DAPT for the primary ischemic end point were not significant (in model 1, HR 0.83, [95%CI 0.43-1.59], $P=0.57$; in model 2, HR 0.66, [95%CI 0.36-1.19], $P=0.17$). The result of the ischemic end point censored by bleeding was also not significant (HR 0.67, [95%CI 0.37-1.23], $P=0.20$). The risks of on-DAPT relative to off-DAPT for the primary bleeding end point were not significant (in model 1, HR 1.00, [95%CI 0.55-1.81], $P=0.997$; in model 2, HR 0.61, [95%CI 0.36-1.03], $P=0.07$). There was no significant interaction between the DAPT score categories and the DAPT status for the primary endpoints (Supplemental Table 6).

In the low DAPT score category, the risks of on-DAPT relative to off-DAPT for the primary ischemic end point were not significant (in model 1, HR 0.96, [95%CI 0.55-1.68], $P=0.90$; in model 2, HR 0.69, [95%CI 0.42-1.15], $P=0.15$). The result of the ischemic end point censored by bleeding was also not significant (HR 0.76, [95%CI 0.45-1.27], $P=0.29$). The risks of on-DAPT relative to off-DAPT for the primary bleeding end point were not significant (in model 1, HR: 1.28, 95%CI, 0.90-1.83, $P=0.17$; in model 2, HR 1.02, [95%CI 0.75-1.40], $P=0.88$, respectively). There was no significant interaction between the DAPT score categories and the DAPT status for the primary endpoints (Supplemental Table 6).

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Figure legends

Supplemental Figure 1. Cumulative incidences of clinical events during the entire 3-year follow-up.

The figures represent the cumulative 3-year incidences of events from baseline in the 12941 patients who discharged alive treated with DES taking DAPT as discharge medication. The cumulative incidences were calculated by the Kaplan-Meier method.

(A) primary ischemic end point; (B) primary bleeding end point; (C) all-cause death; (D) myocardial infarction; (E) stent thrombosis.

DAPT, dual antiplatelet therapy; DES, drug-eluting stent.

Supplemental Figure 2. Cumulative incidences of the primary ischemic end point (A), and the primary bleeding end point (B) by the 13-month landmark analysis; High (2 or higher) versus Middle (1) versus Very Low DAPT (-2 to 0) score categories.

In the additional analysis stratified by the three DAPT score categories (very low [-2 to 0], middle [1] and high [2 or higher] DAPT), the Kaplan-Meier curves diverged in order of the DAPT score, both for the primary ischemic end point and the primary bleeding end point. The cumulative incidences were calculated by the Kaplan-Meier method and the differences were assessed by the log-rank test.

DAPT, dual antiplatelet therapy.

Supplemental Table 1. Protocol, baseline characteristics and results of the studies included in the current analysis.

	CREDO-Kyoto registry cohort-2	RESET	NEXT
Study design, size and duration			
Duration of study	Jan 1 2005 - Dec 31 2007	Feb 22 2010 - Jul 30 2010	May 2 2011 - Nov 11 2011
Design	Registry consecutive patients	RCT	RCT
Study detail	undergoing their first coronary revascularizations	SES vs. EES	EES vs. BES
Study population	13058	3196	3235
Participating centers	26	100	98
Follow-up (year), median (IQR)	5.1 (4.3-5.9)	3.1 (3.0-3.2)	3.1 (3.0-3.3)
Population in the current pooled analysis	6206	2975	3042
Clinical characteristics			
Age	68.1 ± 10.3	68.9 ± 9.7	69.0 ± 9.8
Age ≥75	1817 (29%)	916 (31%)	965 (32%)
Male	4488 (72%)	2300 (77%)	2349 (77%)
Body mass index	23.9 ± 3.4	24.3 ± 3.5	24.2 ± 3.6
Clinical presentation			
Acute myocardial infarction	1277 (21%)	170 (5.7%)	143 (4.7%)
Unstable angina pectoris	396 (6.4%)	368 (12%)	344 (11%)
Stable coronary artery disease	4533 (73%)	2437 (82%)	2555 (84%)
Hypertension	5147 (83%)	2379 (80%)	2467 (81%)
Diabetes	2532 (41%)	1313 (44%)	1386 (46%)
Diabetes on insulin	596 (10%)	305 (10%)	305 (10%)
Current smoking	1769 (29%)	619 (21%)	563 (19%)
History of congestive heart failure	265 (4.3%)	234 (7.9%)	244 (8.0%)
Multivessel disease	3967 (64%)	1365 (46%)	1483 (49%)

LVEF	59.6 ± 12.8	60.0 ± 12.0	60.0 ± 11.5
LVEF <30%	143 (2.7%)	50 (1.9%)	45 (1.7%)
Prior myocardial infarction	766 (12%)	904 (30%)	850 (28%)
Prior PCI	0 (0%)	1459 (49%)	1531 (50%)
Prior stroke	683 (11%)	307 (10%)	306 (10%)
Peripheral vascular disease	435 (7.0%)	247 (8.3%)	118 (3.9%)
eGFR <30 non-HD	197 (3.2%)	56 (1.9%)	75 (2.5%)
HD	231 (3.7%)	140 (4.7%)	146 (4.8%)
Atrial fibrillation	437 (7.0%)	201 (6.8%)	192 (6.3%)
COPD	191 (3.1%)	66 (2.2%)	67 (2.2%)
Liver cirrhosis	137 (2.2%)	18 (0.6%)	20 (0.7%)
Malignancy	495 (8.0%)	185 (6.2%)	216 (7.1%)
Hemoglobin <11.0 g/dL	634 (10%)	342 (12%)	325 (11%)
Platelet <10 ⁵ /μL	77 (1.3%)	35 (1.2%)	44 (1.5%)
Procedural characteristics			
Number of target lesion	1.64 ± 0.85	1.23 ± 0.49	1.25 ± 0.52
Target of unprotected LMCA	250 (4.0%)	72 (2.4%)	85 (2.8%)
Target of chronic total occlusion	895 (14%)	212 (7.1%)	234 (7.7%)
Target of bifurcation lesion	2630 (42%)	668 (22%)	744 (24%)
Side-branch stenting	435 (7.0%)	37 (1.2%)	37 (1.2%)
Total number of stent	2.18 ± 1.40	1.50 ± 0.75	1.58 ± 0.83
Total stent length	47.8 ± 33.3	31.2 ± 19.0	32.8 ± 20.4
Total stent length >28 mm	3796 (61%)	1132 (38%)	1198 (39%)
Minimum stent diameter	2.79 ± 0.37	2.90 ± 0.38	2.90 ± 0.39
Minimum stent diameter <3 mm	3419 (55%)	1341 (45%)	1482 (49%)
Vein graft stenting	0 (0%)	10 (0.3%)	18 (0.6%)
Sirolimus-eluting stent	5772 (93%)	1470 (49%)	2 (0.1%)
Paclitaxel-eluting stent	560 (9.0%)	4 (0.1%)	0 (0%)
Everolimus-eluting stent	3 (0.1%)	1515 (51%)	1524 (50%)
Biolimus eluting stent	71 (1.1%)	0 (0%)	1528 (50%)
Zotarolimus-eluting stent	0 (0%)	7 (0.2%)	5 (0.2%)
Bare-metal stent	1017 (16%)	11 (0.4%)	12 (0.4%)
Discharge medication			
Ticlopidine	5481 (88%)	386 (13%)	425 (14%)

Clopidogrel	717 (12%)	2586 (87%)	2586 (85%)
Cilostazol	1049 (17%)	157 (5.3%)	169 (5.6%)
Statins	3482 (56%)	2321 (78%)	2331 (77%)
β blockers	1820 (29%)	1107 (37%)	1137 (37%)
ACE-I/ARB	3584 (58%)	1840 (62%)	1873 (62%)
Warfarin	486 (7.8%)	238 (8.0%)	216 (7.1%)
SES-use reduced			
Study result	TLR without	EES was	BES was
	increase in death,	noninferior to	noninferior to
	MI, ST, Stroke	SES about both	EES about both
	and bleeding	TLR for 1 year	TLR for 1 year
	regardless of	and Death/MI for	and Death/MI for
	whether AMI or	3 years.	3 years.
	SAP.		

Categorical variables were presented as number (percentage), and continuous variables were presented as mean ± SD.

ACE-I, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; BES, biolimus-eluting stent; COPD, chronic obstructive pulmonary disease; CREDO-Kyoto, Coronary REvascularization Demonstrating Outcome Study in Kyoto; DAPT, dual antiplatelet therapy; EES, everolimus-eluting stent; eGFR, estimated glomerular filtration rate; HD, hemodialysis; LMCA, left main coronary artery; LVEF, left ventricular ejection fraction; MI, myocardial infarction; NEXT, NOBORI Biolimus-Eluting Versus XIENCE/PROMUS Everolimus-Eluting Stent Trial; PCI, percutaneous coronary intervention; RESET, Randomized Evaluation of Sirolimus-Eluting Versus Everolimus-Eluting Stent Trial; SAP, stable angina pectoris; SES, sirolimus-eluting stent; SD, standard deviation; ST, stent thrombosis; TLR, target-lesion revascularization.

Supplemental Table 2. Baseline characteristics of the patients in the high DAPT score category; On-DAPT versus Off-DAPT.

	High DAPT Score Category		P value
	On-DAPT	Off-DAPT	
	at 13 months (N=3149)	at 13 months (N=795)	
(A) Clinical characteristics			
Age	62.1 ± 9.2	61.9 ± 9.0	0.65
Age ≥75*†‡	211 (6.7%)	47 (5.9%)	0.42
Male*†‡	2606 (83%)	653 (82%)	0.68
Body mass index	24.7 ± 3.8	24.4 ± 3.5	0.056
Clinical presentation			
Acute myocardial infarction*†	606 (19%)	232 (29%)	<0.001
Unstable angina pectoris	222 (7.1%)	47 (5.9%)	0.26
Stable coronary artery disease	2321 (73.7%)	516 (64.9%)	<0.001
Hypertension‡	2564 (81%)	632 (79%)	0.22
Diabetes*†‡	2145 (68%)	499 (63%)	0.004
Diabetes on insulin	579 (18%)	104 (13%)	<0.001
Current smoking	1453 (46%)	422 (53%)	<0.001
History of congestive heart failure	490 (16%)	101 (13%)	0.04
Multivessel disease*	1965 (62%)	469 (59%)	0.07
LVEF	55.4 ± 13.8	56.0 ± 14.0	0.32
LVEF <30%	164 (5.2%)	41 (5.0%)	0.84
Prior myocardial infarction*†	1048 (33%)	233 (29%)	0.03
Prior PCI*	1140 (36%)	178 (22%)	<0.001
Prior stroke*‡	320 (10%)	59 (7.4%)	0.02
Peripheral vascular disease	187 (5.9%)	36 (4.5%)	0.11
HD or eGFR <30†‡	270 (8.6%)	53 (6.7%)	0.08
eGFR <30 non-HD*	75 (2.4%)	24 (3.0%)	0.32
HD*	195 (6.2%)	29 (3.7%)	0.004
Atrial fibrillation	166 (5.3%)	55 (6.9%)	0.08
COPD	73 (2.3%)	23 (2.9%)	0.36

Liver cirrhosis*	36 (1.1%)	17 (2.1%)	0.04
Malignancy*	137 (4.4%)	43 (5.4%)	0.21
Hemoglobin <11.0 g/dL*‡	315 (10%)	70 (8.9%)	0.30
Platelet <10 ⁵ /μL*‡	37 (1.2%)	12 (1.5%)	0.46
(B) Procedural characteristics			
Number of target lesion	1.56 ± 0.82	1.55 ± 0.77	0.59
Target of unprotected LMCA*	116 (3.7%)	13 (1.6%)	0.002
Target of chronic total occlusion*	467 (15%)	124 (16%)	0.59
Target of bifurcation lesion	1087 (35%)	276 (35%)	0.92
Side-branch stenting*	157 (5.0%)	36 (4.5%)	0.59
Total number of stent	2.11 ± 1.30	2.04 ± 1.31	0.19
Total number of stent ≥2*	1886 (60%)	450 (57%)	0.09
Total stent length	45.8 ± 31.5	44.6 ± 31.3	0.35
Total stent length >28 mm	1860 (59%)	459 (58%)	0.50
Minimum stent diameter	2.72 ± 0.35	2.72 ± 0.35	0.71
Minimum stent diameter <3 mm*	2188 (70%)	548 (69%)	0.76
Vein graft stenting*	22 (0.7%)	2 (0.3%)	0.11
1st generation drug-eluting stent*	1869 (59%)	582 (73%)	<0.001
Sirolimus-eluting stent	1673 (53%)	553 (70%)	<0.001
Paclitaxel-eluting stent	291 (9.2%)	36 (4.5%)	<0.001
2nd generation drug-eluting stent	1297 (41%)	220 (28%)	<0.001
Everolimus-eluting stent	858 (27%)	147 (18%)	<0.001
Biolimus eluting stent	439 (14%)	73 (9.2%)	<0.001
Zotarolimus-eluting stent	4 (0.13%)	0 (0.0%)	0.18
Bare-metal stent	387 (12%)	100 (13%)	0.83
(C) Discharge medication			
Ticlopidine	1557 (49%)	482 (61%)	<0.001
Clopidogrel	1587 (50%)	309 (39%)	<0.001
Cilostazol*	383 (12%)	161 (20%)	<0.001
Statins†	2283 (73%)	526 (66%)	<0.001
β blockers	1314 (42%)	279 (35%)	<0.001
ACE-I/ARB	2144 (68%)	545 (69%)	0.80
Warfarin*‡	267 (8.5%)	88 (11%)	0.03
(D) Study			

CREDO-Kyoto registry cohort-2	1466 (47%)	508 (64%)	
RESET	833 (26%)	151 (19%)	<0.001
NEXT	850 (27%)	136 (17%)	

Categorical variables were presented as number (percentage), and continuous variables were presented as mean $\pm$ SD.

*Potential variables relevant to the choice of DAPT status at 13 months selected for the logistic regression model to develop propensity score for the choice of DAPT at 13 months.

†Potential variables selected in the multivariable analysis of the Cox regression models comparing on-DAPT with off-DAPT for the primary ischemic end point.

‡Potential variables selected in the multivariable analysis of the Cox regression models comparing on-DAPT with off-DAPT for the primary bleeding end point.

ACE-I, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blockers; COPD, chronic obstructive pulmonary disease; CREDO-Kyoto, Coronary REvascularization Demonstrating Outcome Study in Kyoto; DAPT, dual antiplatelet therapy; eGFR, estimated glomerular filtration rate; HD, hemodialysis; LMCA, left main coronary artery; LVEF, left ventricular ejection fraction; NEXT, NOBORI Biolimus-Eluting Versus XIENCE/PROMUS Everolimus-Eluting Stent Trial; PCI, percutaneous coronary intervention; RESET, Randomized Evaluation of Sirolimus-Eluting Versus Everolimus-Eluting Stent Trial; SD, standard deviation.

Supplemental Table 3. Baseline characteristics of the patients in the low DAPT score category: On-DAPT versus Off-DAPT.

	Low DAPT Score Category		P value
	On-DAPT	Off-DAPT	
	at 13 months (N=6222)	at 13 months (N=2057)	
(A) Clinical characteristics			
Age	71.8 ± 8.8	71.1 ± 9.3	0.002
Age ≥75*†‡	2623 (42%)	817 (40%)	0.051
Male*†‡	4445 (71%)	1433 (70%)	0.13
Body mass index	23.9 ± 3.4	23.6 ± 3.2	<0.001
Clinical presentation			
Acute myocardial infarction*†	508 (8.2%)	244 (12%)	<0.001
Unstable angina pectoris	631 (10.1%)	208 (10.1%)	0.97
Stable coronary artery disease	5083 (81.7%)	1605 (78.0%)	<0.001
Hypertension‡	5119 (82%)	1678 (82%)	0.48
Diabetes*†‡	2023 (33%)	564 (27%)	<0.001
Diabetes on insulin	411 (6.6%)	112 (5.4%)	0.057
Current smoking	771 (12%)	305 (15%)	0.005
History of congestive heart failure	117 (1.9%)	35 (1.7%)	0.60
Multivessel disease*	3312 (53%)	1069 (52%)	0.32
LVEF	61.6 ± 10.9	62.2 ± 11.0	0.051
LVEF <30%	24 (0.4%)	10 (0.5%)	0.54
Prior myocardial infarction*†	1003 (16%)	236 (11%)	<0.001
Prior PCI*	1437 (23%)	235 (11%)	<0.001
Prior stroke*‡	724 (12%)	193 (9.4%)	0.004
Peripheral vascular disease	449 (7.2%)	128 (6.2%)	0.12
HD or eGFR <30†‡	409 (6.6%)	113 (5.5%)	0.08
eGFR <30 non-HD*	173 (2.8%)	56 (2.7%)	0.89
HD*	236 (3.8%)	57 (2.8%)	0.03
Atrial fibrillation	435 (7.0%)	174 (8.5%)	0.03
COPD	159 (2.6%)	69 (3.4%)	0.06

Liver cirrhosis*	72 (1.2%)	50 (2.4%)	<0.001
Malignancy*	520 (8.4%)	196 (9.5%)	0.10
Hemoglobin <11.0 g/dL*‡	718 (12%)	198 (9.7%)	0.02
Platelet <10 ⁵ /μL*‡	78 (1.3%)	29 (1.4%)	0.59
(B) Procedural characteristics			
Number of target lesion	1.38 ± 0.67	1.40 ± 0.71	0.20
Target of unprotected LMCA*	228 (3.7%)	50 (2.4%)	0.005
Target of chronic total occlusion*	556 (8.9%)	194 (9.4%)	0.50
Target of bifurcation lesion	2015 (32%)	664 (32%)	0.93
Side-branch stenting*	238 (3.8%)	78 (3.8%)	0.95
Total number of stent	1.75 ± 1.10	1.77 ± 1.16	0.48
Total number of stent ≥2*	2816 (45%)	900 (44%)	0.23
Total stent length	37.2 ± 26.3	38.0 ± 27.8	0.30
Total stent length >28 mm	2882 (46%)	925 (45%)	0.29
Minimum stent diameter	2.90 ± 0.38	2.90 ± 0.38	0.91
Minimum stent diameter <3 mm*	2664 (43%)	842 (41%)	0.13
Vein graft stenting*	4 (0.1%)	1 (0.1%)	0.80
1st generation drug-eluting stent*	3654 (58.7%)	1525 (74.1%)	<0.001
Sirolimus-eluting stent	3519 (57%)	1499 (73%)	<0.001
Paclitaxel-eluting stent	201 (3.2%)	36 (1.8%)	<0.001
2nd generation drug-eluting stent	2586 (41.6%)	533 (25.9%)	<0.001
Everolimus-eluting stent	1708 (28%)	329 (16%)	<0.001
Biolimus eluting stent	881 (14%)	206 (10%)	<0.001
Zotarolimus-eluting stent	8 (0.1%)	0 (0.0%)	0.03
Bare-metal stent	399 (6.4%)	154 (7.5%)	0.09
(C) Discharge medication			
Ticlopidine	2968 (48%)	1285 (62%)	<0.001
Clopidogrel	3240 (52%)	753 (37%)	<0.001
Cilostazol*	572 (9.2%)	259 (13%)	<0.001
Statins†	4076 (66%)	1249 (61%)	<0.001
β blockers	1889 (30%)	582 (28%)	0.08
ACE-I/ARB	3525 (57%)	1083 (53%)	0.002
Warfarin*‡	425 (6.8%)	160 (7.8%)	0.15
(D) Study			

CREDO-Kyoto registry cohort-2	2840 (46%)	1392 (68%)	
RESET	1699 (27%)	292 (14%)	<0.001
NEXT	1683 (27%)	373 (18%)	

Categorical variables were presented as number (percentage), and continuous variables were presented as mean $\pm$ SD.

*Potential variables relevant to the choice of DAPT status at 13 months selected for the logistic regression model to develop propensity score for the choice of DAPT at 13 months.

†Potential variables selected in the multivariable analysis of the Cox regression models comparing on-DAPT with off-DAPT for the primary ischemic end point.

‡Potential variables selected in the multivariable analysis of the Cox regression models comparing on-DAPT with off-DAPT for the primary bleeding end point.

ACE-I, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blockers; COPD, chronic obstructive pulmonary disease; CREDO-Kyoto, Coronary REvascularization Demonstrating Outcome Study in Kyoto; DAPT, dual antiplatelet therapy; eGFR, estimated glomerular filtration rate; HD, hemodialysis; LMCA, left main coronary artery; LVEF, left ventricular ejection fraction; NEXT, NOBORI Biolimus-Eluting Versus XIENCE/PROMUS Everolimus-Eluting Stent Trial; PCI, percutaneous coronary intervention; RESET, Randomized Evaluation of Sirolimus-Eluting Versus Everolimus-Eluting Stent Trial; SD, standard deviation.

Supplemental Table 4. Patient characteristics of the propensity score-matched cohort in the high DAPT score category: On-DAPT versus Off-DAPT.

High DAPT score category	Propensity score-matched cohort		P value
	On-DAPT	Off-DAPT	
	at 13 months (N = 795)	at 13 months (N = 795)	
(A) Clinical characteristics			
Age	60.7 ± 9.4	61.9 ± 9.0	0.006
Age ≥75*	40 (5.0%)	47 (5.9%)	0.44
Male*	660 (83.0%)	653 (82%)	0.64
Body mass index	24.5 ± 3.5	24.4 ± 3.5	0.40
Clinical presentation			
Acute myocardial infarction*	243 (31%)	232 (29%)	0.55
Unstable angina pectoris	43 (5.4%)	47 (5.9%)	0.66
Stable coronary artery disease	509 (64%)	516 (65%)	0.71
Hypertension	649 (82%)	632 (80%)	0.28
Diabetes*	496 (63%)	499 (63%)	0.88
Diabetes on insulin	120 (15%)	104 (13%)	0.25
Current smoking	415 (52%)	422 (53%)	0.73
History of congestive heart failure	91 (11%)	101 (13%)	0.44
Multivessel disease*	477 (60%)	469 (59%)	0.68
LVEF	55.2 ± 13.8	56.2 ± 13.8	0.18
LVEF <30%	43 (6.2%)	40 (5.7%)	0.70
Prior myocardial infarction*	217 (27%)	233 (29%)	0.37
Prior PCI*	184 (23%)	178 (22%)	0.72
Prior stroke*	60 (7.6%)	59 (7.4%)	0.92
Peripheral vascular disease	39 (4.9%)	36 (4.5%)	0.72
HD or eGFR <30	51 (6.4%)	53 (6.7%)	0.84
eGFR <30 non-HD*	24 (3.0%)	24 (3.0%)	1.00
HD*	27 (3.4%)	29 (3.7%)	0.79
Atrial fibrillation	34 (4.3%)	55 (6.9%)	0.02
COPD	14 (1.8%)	23 (2.9%)	0.13

Liver cirrhosis*	19 (2.4%)	17 (2.1%)	0.74
Malignancy*	30 (3.8%)	43 (5.4%)	0.12
Hemoglobin <11.0 g/dL*	67 (8.6%)	70 (8.9%)	0.84
Platelet <10 ⁵ /μL*	13 (1.7%)	12 (1.5%)	0.82
(B) Procedural characteristics			
Number of target lesion	1.56 ± 0.81	1.55 ± 0.77	0.73
Target of unprotected LMCA*	9 (1.1%)	13 (1.6%)	0.39
Target of chronic total occlusion*	128 (16%)	124 (16%)	0.78
Target of bifurcation lesion	286 (36%)	276 (35%)	0.60
Side-branch stenting*	35 (4.4%)	36 (4.5%)	0.90
Total number of stent	2.07 ± 1.31	2.04 ± 1.31	0.70
Total number of stent ≥2*	449 (56%)	450 (57%)	0.96
Total stent length	44.7 ± 31.2	44.6 ± 31.3	0.94
Total stent length >28 mm	453 (57%)	459 (58%)	0.76
Minimum stent diameter	2.72 ± 0.34	2.72 ± 0.35	0.90
Minimum stent diameter <3 mm*	553 (70%)	548 (69%)	0.79
Vein graft stenting*	1 (0.1%)	2 (0.3%)	0.56
1st generation drug-eluting stent*	591 (74.3%)	582 (73%)	0.61
Sirolimus-eluting stent	529 (67%)	553 (70%)	0.20
Paclitaxel-eluting stent	92 (12%)	36 (4.5%)	<0.001
2nd generation drug-eluting stent	208 (26%)	220 (28%)	0.50
Everolimus-eluting stent	128 (16%)	147 (18%)	0.21
Biolimus-eluting stent	80 (10%)	73 (9.2%)	0.55
Zotarolimus-eluting stent	0 (0.0%)	0 (0.0%)	NA
Bare-metal stent	115 (14%)	100 (13%)	0.27
(C) Discharge medication			
Ticlopidine	493 (62%)	482 (61%)	0.57
Clopidogrel	301 (38%)	309 (39%)	0.68
Cilostazol*	165 (21%)	161 (20%)	0.80
Statins†	569 (72%)	526 (66%)	0.02
β blockers	331 (42%)	279 (35%)	0.007
ACE-I/ARB	560 (70%)	545 (69%)	0.41
Warfarin*	72 (9.1%)	88 (11%)	0.18
(D) Study			

CREDO-Kyoto registry cohort-2	494 (62%)	508 (64%)	
RESET	167 (21%)	151 (19%)	0.60
NEXT	134 (17%)	136 (17%)	

Categorical variables were presented as number (percentage), and continuous variables were presented as mean $\pm$ SD.

*Potential variables relevant to the choice of DAPT status at 13 months selected for the logistic regression model to develop propensity score for the choice of DAPT at 13 months. ACE-I, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blockers; COPD, chronic obstructive pulmonary disease; CREDO-Kyoto, Coronary REvascularization Demonstrating Outcome Study in Kyoto; DAPT, dual antiplatelet therapy; eGFR, estimated glomerular filtration rate; HD, hemodialysis; LMCA, left main coronary artery; LVEF, left ventricular ejection fraction; NEXT, NOBORI Biolimus-Eluting Versus XIENCE/PROMUS Everolimus-Eluting Stent Trial; PCI, percutaneous coronary intervention; RESET, Randomized Evaluation of Sirolimus-Eluting Versus Everolimus-Eluting Stent Trial; SD, standard deviation.

Supplemental Table 5. Patient characteristics of the propensity score-matched cohort in the low DAPT score category: On-DAPT versus Off-DAPT.

Low DAPT score category	Propensity score-matched cohort		P value
	On-DAPT	Off-DAPT	
	at 13 months (N = 2057)	at 13 months (N = 2057)	
(A) Clinical characteristics			
Age	70.9 ± 8.9	71.1 ± 9.3	0.55
Age ≥75*	775 (38%)	817 (40%)	0.18
Male*	1465 (71%)	1433 (70%)	0.27
Body mass index	23.9 ± 3.4	23.6 ± 3.2	0.003
Clinical presentation			
Acute myocardial infarction*	236 (11%)	244 (12%)	0.70
Unstable angina pectoris	199 (10%)	208 (10%)	0.64
Stable coronary artery disease	1622 (79%)	1605 (78%)	0.52
Hypertension	1677 (82%)	1678 (82%)	0.97
Diabetes*	553 (27%)	564 (27%)	0.70
Diabetes on insulin	109 (5.3%)	112 (5.4%)	0.84
Current smoking	310 (15%)	305 (15%)	0.83
History of congestive heart failure	34 (1.7%)	35 (1.7%)	0.90
Multivessel disease*	1070 (52%)	1069 (52%)	0.98
LVEF	61.8 ± 10.9	62.3 ± 10.9	0.16
LVEF <30%	7 (0.4%)	10 (0.6%)	0.46
Prior myocardial infarction*	243 (12%)	236 (11%)	0.73
Prior PCI*	228 (11%)	235 (11%)	0.73
Prior stroke*	180 (8.8%)	193 (9.4%)	0.48
Peripheral vascular disease	120 (5.8%)	128 (6.2%)	0.60
HD or eGFR <30	91 (4.4%)	113 (5.5%)	0.11
eGFR <30 non-HD*	42 (2.0%)	56 (2.7%)	0.15
HD*	49 (2.4%)	57 (2.8%)	0.43
Atrial fibrillation	166 (8.1%)	174 (8.5%)	0.65
COPD	50 (2.4%)	69 (3.4%)	0.08

Liver cirrhosis*	46 (2.2%)	50 (2.4%)	0.68
Malignancy*	174 (8.5%)	196 (9.5%)	0.23
Hemoglobin <11.0 g/dL*	169 (8.3%)	198 (9.7%)	0.10
Platelet <10 ⁵ /μL*	22 (1.1%)	29 (1.4%)	0.32
(B) Procedural characteristics			
Number of target lesion	1.39 ± 0.68	1.40 ± 0.71	0.50
Target of unprotected LMCA*	47 (2.3%)	50 (2.4%)	0.76
Target of chronic total occlusion*	167 (8.1%)	194 (9.4%)	0.14
Target of bifurcation lesion	699 (34%)	664 (32%)	0.25
Side-branch stenting*	74 (3.6%)	78 (3.8%)	0.74
Total number of stent	1.74 ± 1.14	1.77 ± 1.16	0.53
Total number of stent ≥2*	891 (43%)	900 (44%)	0.78
Total stent length	37.4 ± 27.2	38.0 ± 27.8	0.52
Total stent length >28 mm	932 (45%)	925 (45%)	0.83
Minimum stent diameter	2.90 ± 0.38	2.90 ± 0.38	0.63
Minimum stent diameter <3 mm*	839 (41%)	842 (41%)	0.92
Vein graft stenting*	0 (0.0%)	1 (0.1%)	0.32
1st generation drug-eluting stent*	1520 (74%)	1525 (74%)	0.86
Sirolimus-eluting stent	1460 (71%)	1499 (73%)	0.18
Paclitaxel-eluting stent	81 (3.9%)	36 (1.8%)	<0.001
2nd generation drug-eluting stent	546 (27%)	533 (26%)	0.65
Everolimus-eluting stent	361 (18%)	329 (16%)	0.18
Biolimus-eluting stent	185 (9.0%)	206 (10%)	0.26
Zotarolimus-eluting stent	3 (0.2%)	0 (0.0%)	0.08
Bare-metal stent	160 (7.8%)	154 (7.5%)	0.72
(C) Discharge medication			
Ticlopidine	1187 (58%)	1285 (62%)	0.002
Clopidogrel	862 (42%)	753 (37%)	0.001
Cilostazol*	233 (11%)	259 (13%)	0.21
Statins	1291 (63%)	1249 (61%)	0.18
β blockers	602 (29%)	582 (28%)	0.49
ACE-I/ARB	1145 (56%)	1083 (53%)	0.052
Warfarin*	156 (7.6%)	160 (7.8%)	0.81
(D) Study			

CREDO-Kyoto registry cohort-2	1237 (60%)	1392 (68%)	
RESET	460 (22%)	292 (14%)	<0.001
NEXT	360 (18%)	373 (18%)	

Categorical variables were presented as number (percentage), and continuous variables were presented as mean $\pm$ SD.

*Potential variables relevant to the choice of DAPT status at 13 months selected for logistic regression model to develop propensity score for the choice of DAPT at 13 months.

ACE-I, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blockers; COPD, chronic obstructive pulmonary disease; CREDO-Kyoto, Coronary REvascularization Demonstrating Outcome Study in Kyoto; DAPT, dual antiplatelet therapy; eGFR, estimated glomerular filtration rate; HD, hemodialysis; LMCA, left main coronary artery; LVEF, left ventricular ejection fraction; NEXT, NOBORI Biolimus-Eluting Versus XIENCE/PROMUS Everolimus-Eluting Stent Trial; PCI, percutaneous coronary intervention; RESET, Randomized Evaluation of Sirolimus-Eluting Versus Everolimus-Eluting Stent Trial; SD, standard deviation.

Supplemental Table 6. Risks of on-DAPT relative to off-DAPT for clinical outcomes.

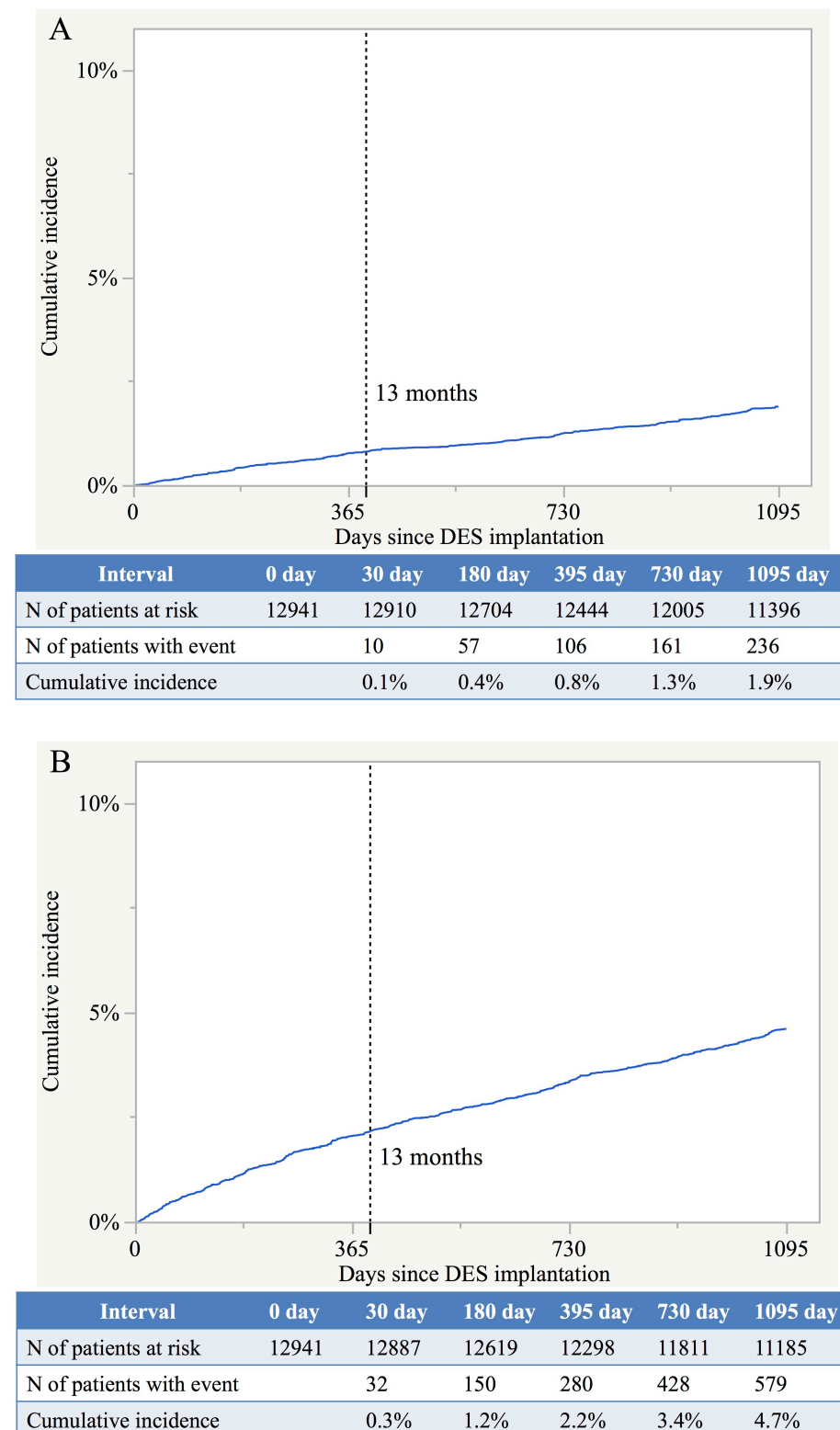
	Model 1			Model 2		
	DAPT status at 13 months for On versus Off approach			DAPT status beyond 13 months as time-updated covariate		
(A) DAPT score ≥2	Adjusted HR		P value	Adjusted HR		P value
	[95% CI]			[95% CI]		
Primary ischemic end point (MI+Definite/Probable ST)	0.83	[0.43-1.59]	0.57	0.66	[0.36-1.19]	0.17
Primary ischemic end point censored by bleeding	NA	NA	NA	0.67	[0.37-1.23]	0.20
Primary bleeding end point (GUSTO Moderate/Severe)	1.00	[0.55-1.81]	0.997	0.61	[0.36-1.03]	0.07
(B) DAPT score <2	Adjusted HR		P value	Adjusted HR		P value
	[95% CI]			[95% CI]		
Primary ischemic end point (MI+Definite/Probable ST)	0.96	[0.55-1.68]	0.90	0.69	[0.42-1.15]	0.15
Primary ischemic end point censored by bleeding	NA	NA	NA	0.76	[0.45-1.27]	0.29
Primary bleeding end point (GUSTO Moderate/Severe)	1.28	[0.90-1.83]	0.17	1.02	[0.75-1.40]	0.88
(C) Interaction	Interaction P			Interaction P		
Primary ischemic end point (MI+Definite/Probable ST)	0.84			0.95		
Primary ischemic end point censored by bleeding	NA			0.77		
Primary bleeding end point (GUSTO Moderate/Severe)	0.44			0.10		

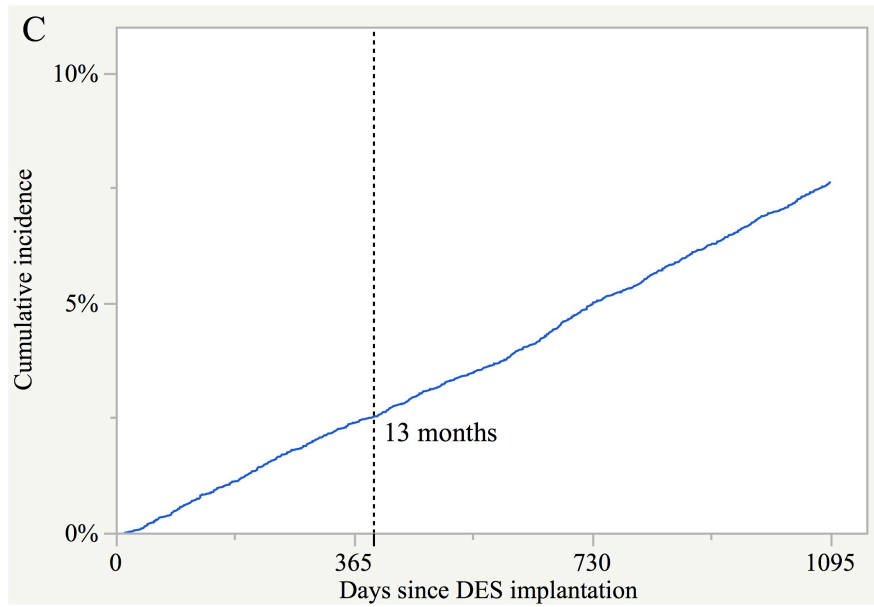
The hazard ratios represent the risks of on-DAPT status relative to off-DAPT status for each clinical event. Interactions between DAPT status and DAPT score categories are shown in Interaction P columns. In model 1, DAPT status at 13 months was incorporated into the

multivariable Cox regression model. In model 2, DAPT status beyond 13 months was incorporated as a time-updated covariate into the multivariable Cox regression model. The risk-adjusting covariates are listed in Supplemental Table 2 and 3.

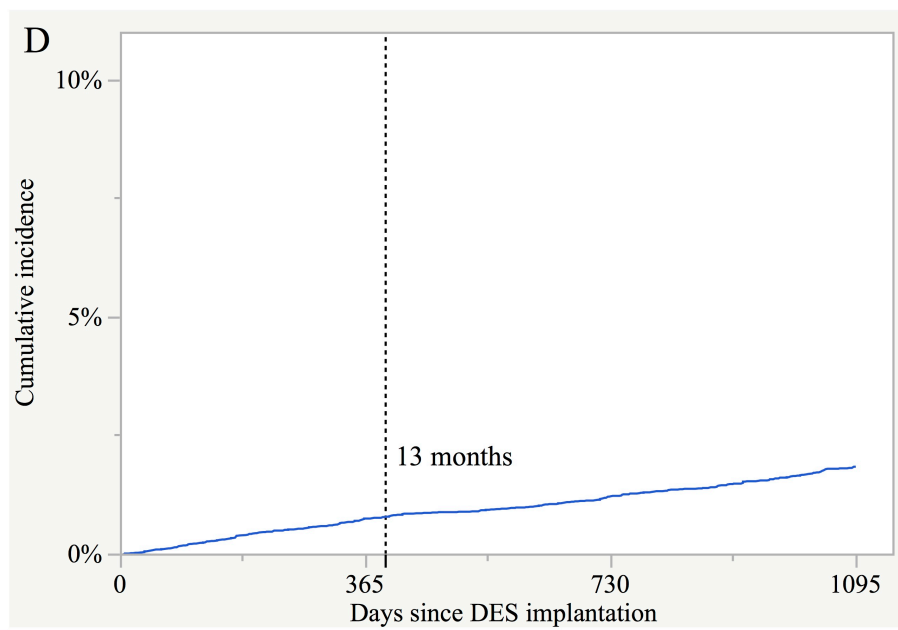
CI, confidence intervals; DAPT, dual antiplatelet therapy; GUSTO, Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries; HR, hazard ratio; MI, myocardial infarction; ST, stent thrombosis.

Supplemental Figure 1. Cumulative incidences of clinical events during the entire 3-year follow-up.

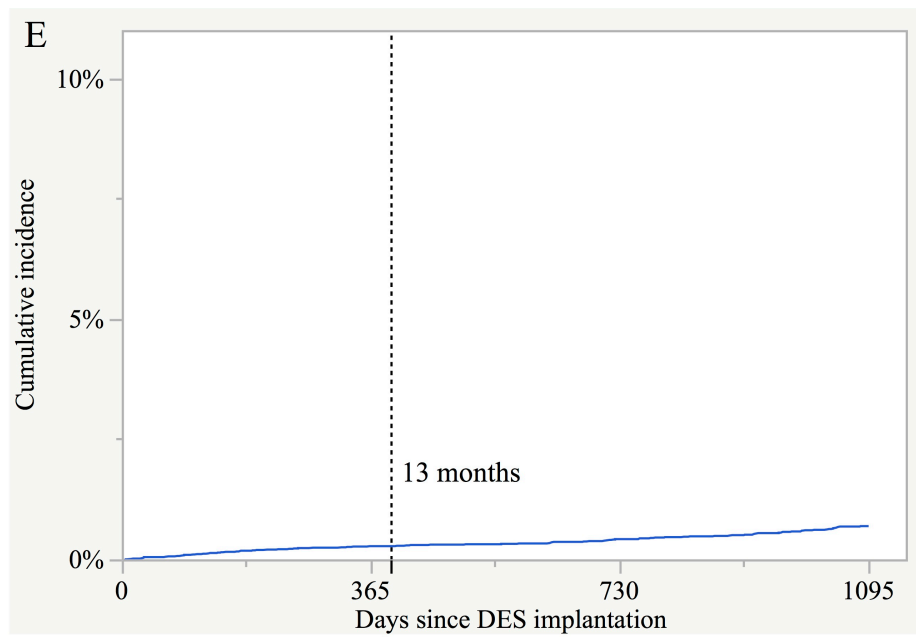




Interval	0 day	30 day	180 day	395 day	730 day	1095 day
N of patients at risk	12941	12918	12752	12529	12128	11575
N of patients with event		11	148	329	646	977
Cumulative incidence		0.1%	1.2%	2.6%	5.0%	7.6%

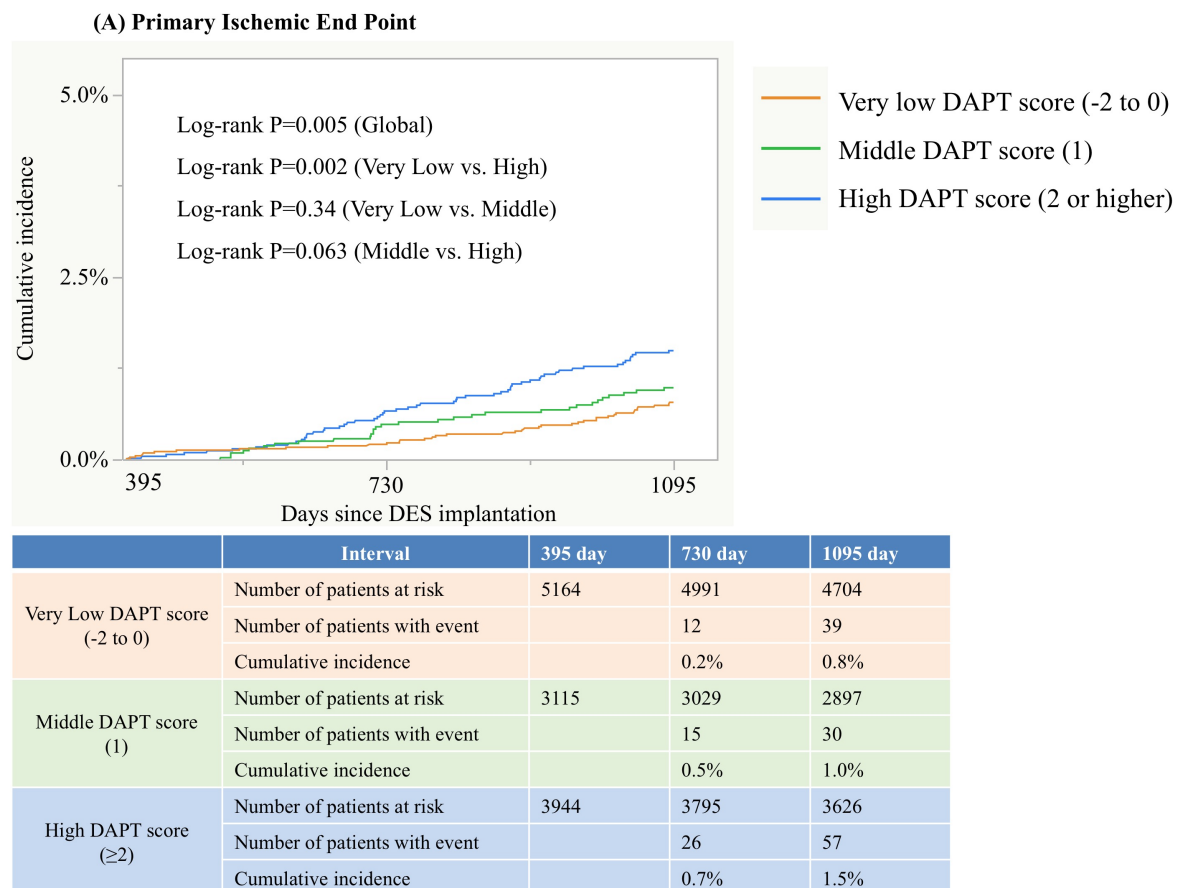


Interval	0 day	30 day	180 day	395 day	730 day	1095 day
N of patients at risk	12941	12911	12705	12445	12007	11398
N of patients with event		18	53	102	156	229
Cumulative incidence		0.1%	0.4%	0.8%	1.2%	1.9%

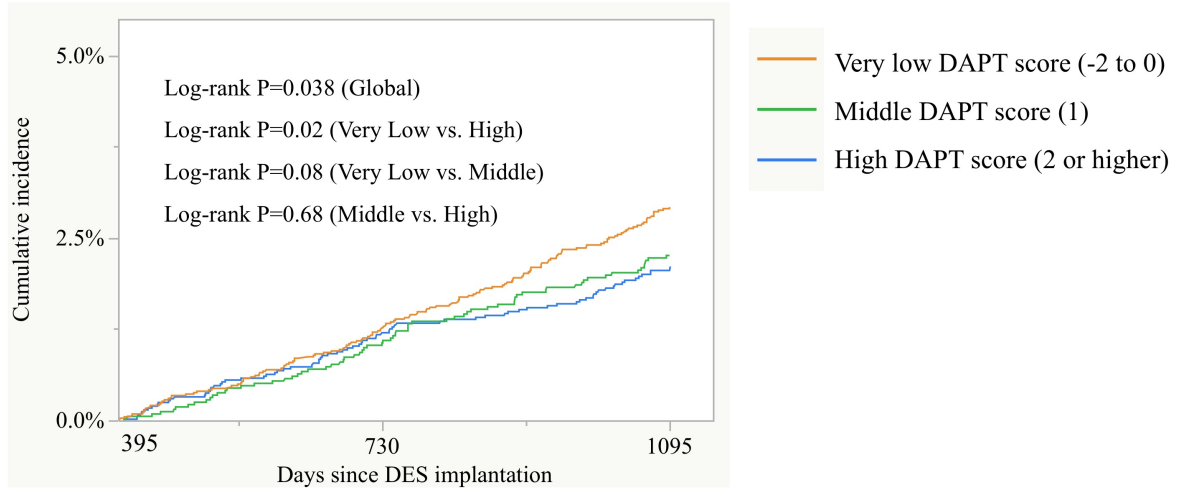


Interval	0 day	30 day	180 day	395 day	730 day	1095 day
N of patients at risk	12941	12912	12730	12502	12093	11511
N of patients with event		8	26	38	56	88
Cumulative incidence		0.1%	0.2%	0.3%	0.4%	0.7%

Supplemental Figure 2. Cumulative incidences of the primary ischemic end point (A), and the primary bleeding end point (B) by the 13-month landmark analysis; High (2 or higher) versus Middle (1) versus Very Low DAPT (-2 to 0) score categories.



(B) Primary Bleeding End Point



	Interval	395 day	730 day	1095 day
Very Low DAPT score (-2 to 0)	Number of patients at risk	5164	4964	4638
	Number of patients with event		65	146
	Cumulative incidence		1.3%	2.9%
Middle DAPT score (1)	Number of patients at risk	3115	3015	2876
	Number of patients with event		34	69
	Cumulative incidence		1.1%	2.3%
High DAPT score (≥2)	Number of patients at risk	3944	3778	3612
	Number of patients with event		47	81
	Cumulative incidence		1.2%	2.1%