Effect of Perioperative Antiplatelet Therapy on Outcomes in Patients With Drug-Eluting Stents Undergoing Elective Noncardiac Surgery

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We investigated the association of perioperative antiplatelet therapy (APT) and outcomes in patients with drug-eluting stent (DES) placement for noncardiac surgery (NCS). In consecutive 23,358 patients who underwent percutaneous coronary interventions between 2005 and 2016, total of 2,179 patients that required 2,179 elective NCS after DES placement were retrospectively analyzed. A net adverse clinical event (NACE), composite of death, myocardial infarction, stent thrombosis, and major bleeding, was assessed at 30 days. Of 2,179 patients, 937 patients (43%) underwent NCS with discontinuation of APT. For overall, NACE occurred in 10 patients who discontinued APT (1.1%) and 22 patients who continued APT (1.8%) without significant differences (hazard ratio [HR] 0.60, 95% confidence interval [CI] 0.28 to 1.27, p = 0.182). Also, adjusted NACE event rates were not different between groups for overall NCSs (adjusted HR 0.76, 95% CI 0.38 to 1.52, p = 0.440), for NCSs >1, ≤12 months after DES, and for NCSs >12 months after DES. Our findings persisted (adjusted HR 1.26, 95% CI 0.51 to 3.10, p = 0.618) when those who continued dual-APT were excluded from the continuation of APT group due to a higher tendency of NACE compared with those who continued single-APT (adjusted HR 2.26, 95% CI 0.98 to 5.21, p = 0.055). However, the patients who discontinued APT for >7 days had a significantly higher NACE than those who discontinued for ≤7 days (adjusted HR 6.93, 95% CI 2.16 to 22.24, p = 0.001). In conclusion, discontinuation of APT may not be associated with higher NACEs 30 days postsurgery compared with continuation of APT, when APT was discontinued for ≤7 days in patients undergoing elective NCS after DES implantation. **(Am J Cardiol 2019;123:1414−1421)**

Percutaneous coronary intervention (PCI) with a drug-eluting stent (DES) is the most common strategy for myocardial revascularization.[1] However, patients treated with DES continue to have concerns regarding stent thrombosis, necessitating dual-antiplatelet therapy (APT) until complete endothelialization has occurred, followed by a persistent single-APT.[2] In DES-treated patients with APT, the need for noncardiac surgery (NCS) occurs in 11% to 34% of cases.[3−6] Thus, cardiologists, surgeons, primary physicians, and anesthesiologists frequently make decisions to continue or discontinue APT before NCS for DES-treated patients. However, there is no randomized clinical trials that evaluate the value of perioperative APT, and small observational studies show conflicting results.[7−14] Current guidelines recommend that aspirin be continued in most clinical situations, as it provides benefits that outweigh the bleeding risk for patients with dual-APT, although the evidence supporting these guidelines is weak.[2,15,16] We evaluated whether discontinuation of APT before elective NCS was associated with a higher net adverse clinical event (NACE) 30 days postsurgery in DES-treated patients.

Methods

This study was conducted at an academic tertiary center, the 2,048-bed Severance Hospital (Seoul, Korea). The Institutional Review Board at the Severance Hospital of the Yonsei University Health System approved this study. Total of 23,358 consecutive patients who underwent PCI between November 2005 and December 2016 in our hospital were initially identified from the Korean Multicenter Angioplasty Team (KOMATE) registry (Figure 1). The KOMATE registry was designed to enroll patients that underwent PCI at multicenters in Korea and collect demographic, procedural, and clinical outcomes using case report forms.[17] Of 23,358 patients who received PCI, 2,300

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See page 1420 for disclosure information.

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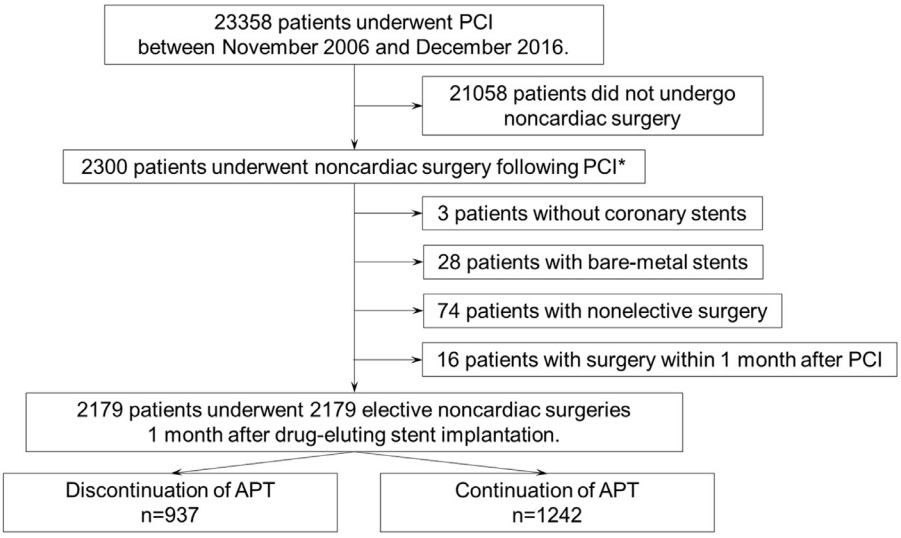

Figure 1. **Flowchart of the study population**. *When a patient underwent more than 2 operations after PCI, the first operation after PCI was included in our analyses. APT = antiplatelet therapy; PCI = percutaneous coronary intervention.

patients required NCS after DES implantation. When a patient underwent more than 2 operations after PCI, the first operation after PCI was included in our analyses. In these 2,300 patients, 3 without coronary stents, 28 with bare-metal stents, and 74 with nonelective surgery were excluded. Sixteen surgeries within 1 month after PCI were also excluded because it is generally agreed to avoid surgery in the first month following PCI.[3,5,14,16] Thus, the final population consisted of 2,179 patients with 2,179 elective noncardiac surgeries; vascular surgery (n = 97), orthopedic and/or neurologic surgery (n = 517); thoracic and/or abdominal and/or urologic surgery (n = 840); ear, nose, and thoracic and/or eye and/or other surgery (n = 725). Within 6 months after PCI, 259 NCSs were performed for malignancy (n = 187), infection (n = 42), trauma (n = 22), and others (n = 8).

The data regarding the procedural characteristics of PCI were obtained from the registry.[17] Through electronic medical record review, data on demographics and pre-existing medical conditions at surgery, surgical outcomes, and perioperative medications were collected by the first 2 authors (SJH, MJK). The inpatient and outpatient medical records were reviewed to obtain follow-up data for patients in our hospital. In this study, continuation or discontinuation of APT before NCS was firstly recommended by cardiologists, and finally determined by both surgeons and anesthesiologists. Thus, this decision was determined mainly by the preferences of cardiologists, surgeons, and anesthesiologists. These decisions and the types of perioperative APT were reviewed by the consultation sheets of the medical records, the physicians' medication orders, and the medication administration records.

Clinical outcomes were collected for up to 30 days after NCS in all patients. All-cause death, myocardial infarction, stent thrombosis, and major bleeding were assessed as clinical outcomes. NACE was defined as a composite of all-cause death, myocardial infarction, stent thrombosis, and major bleeding. Myocardial infarction was defined according to the following parameters: presence of clinical symptoms, electrocardiographic changes or abnormal imaging findings indicative of myocardial infarction, and an increase in the creatine kinase myocardial band fraction above the upper normal limits or an increase in troponin-T/troponin-I above the 99th percentile of the upper normal limit. Definite, probable, and possible stent thrombosis was also defined according to the recommendations of the Academic Research Consortium. Major bleeding was defined according to the International Society of Thrombosis and Hemostasis.[18]

Continuous variables were reported as mean ± standard deviation and compared with the Student's *t* Test. Categorical variables were reported as numbers and percentages, and compared using the chi-square test or Fisher's exact test. In order to reduce the impact of selection bias and potential confounding, the inverse probability of treatment weighting after stabilization and trimming was used. Propensity scores were estimated using multiple logistic regression analysis, and the covariates in the propensity score model included risk factors significantly different between the treatment groups (discontinuation of APT vs continuation of APT); age, diabetes, chronic kidney disease, preoperative hemoglobin, type of DES, and type of surgeries. The c-statistics was 0.7 (Hosmer-Lemeshow goodness of fit, p = 0.259). The significance level was set at 0.05 for the 2-sided test. All statistical analyses were carried out using SAS (version 9.4, SAS Inc., Cary, North Carolina).

Results

In 2,179 patients, 937 (43%) underwent NCS after discontinuation of APT. Of 937 patients who discontinued APT, 341 (36.4%) had been treated with dual-APT, and these patients discontinued both antiplatelet agents. Single-APT restarted in 617 patients (66%) ≤2 days, in 76 patients (8%) >2, ≤5 days, and in 32 patients (3%) >5 days after

NCS. Dual-APT restarted in 89 patients (9%) ≤2 days, in 53 patients (6%) >2, ≤5 days, and in 70 patients (7%) >5 days after NCS. Of the 1,242 patients who continued APT with 591 patients (47.6%) treated with dual-APT, dual-APT and single-APT were continued in 460 patients (37.0%) and 782 patients (63%, aspirin: n = 735 and clopidogrel: n = 47). Overall, warfarin had been treated for 42 patients (31 patients for atrial fibrillation, 8 for mechanical valves, and 3 for other reasons), and discontinued either 2 or 3 days before NCS. Heparin as a bridge was maintained for 11 patients with high thrombotic risk. Baseline characteristics according to perioperative APT strategy (discontinuation vs continuation of APT) are presented in Table 1 for overall, NCS >1, ≤12 months after DES placement, and NCS >12 months after DES placement. After inverse probability weighting adjustment, patients were well matched (Supplemental Table 1).

Clinical outcomes are summarized in Table 2. For overall, NACE occurred in 10 patients who discontinued APT (1.1%) and 22 patients who continued APT (1.8%) without significant differences (hazard ratio [HR] 0.60, 95% confidence interval [CI] 0.28 to 1.27, p = 0.182). Also, adjusted NACE event rates were not different between groups (adjusted HR 0.76, 95% CI 0.38 to 1.52, p = 0.440; Figure 2). A composite of death, myocardial infarction, and stent thrombosis was not high in patients with discontinuation of APT compared with those with continuation of APT. Each clinical outcome of all-cause of death, myocardial infarction, stent thrombosis (1 probable stent thrombosis in patient who discontinued APT; 1 definite stent thrombosis in patient who continued APT), or major bleeding (2 surgery-related bleeding in patients who discontinued APT; 2 surgery-related bleeding and 1 non-surgery-related bleeding in patients who continued APT) did not differ between groups. These findings were consistent across the different NCS timing after DES implantation. Adjusted NACE were not different between groups as for NCS >1, ≤12 months after DES, and as for NCS >12 months after DES (Table 2). Also, 259 patients underwent NCS ≤6 months after DES. In 58 patients who discontinued APT, 23 patients implanted DES for acute coronary syndrome at the time of PCI, and NACE occurred in 1 patient.

When patients who continued dual-APT (n = 460) were excluded from the continuation of APT group due to a higher tendency of NACE compared with those who continued single-APT (adjusted HR 2.26, 95% CI 0.98 to 5.21, p = 0.055) (Supplemental Table 2) (Figure 2), our findings persisted. Thus, there were no significant differences as for NACE between the patients who discontinued and those who continued single-APT (1.1% vs 1.0%, adjusted HR 1.26, 95% CI 0.51 to 3.10, p = 0.618) (Table 3, Figure 2). Clinical and angiographic characteristics before and after inverse probability weighting according to different strategies of APT were also provided in Supplemental Table 3 and Supplemental Table 4. However, when patients who discontinued APT were further classified according to the total discontinued durations of APT (Table 4), those with discontinuation of APT for >7 days had significantly higher NACEs than those with discontinuation of APT for ≤7 days (adjusted HR 6.93, 95% CI 2.16 to 22.24, p = 0.001; Figure 2). Characteristics

Table 1
Baseline characteristics

Variable	Overall			Noncardiac surgery after DES implantation ≤12 months			Noncardiac surgery after DES implantation >12 months		
	Discontinuation of APT (n = 937)	Continuation of APT (n = 1,242)	p Value	Discontinuation of APT (n = 150)	Continuation of APT (n = 383)	p Value	Discontinuation of APT (n=787)	Continuation of APT (n=859)	p Value
Age (years)	67 ± 9	69 ± 10	0.002	67 ± 9	67 ± 11	0.837	68±9	69±9	<0.001
Men	631 (67%)	824 (66%)	0.624	107 (71%)	265 (69%)	0.628	524 (67%)	559 (65%)	0.520
Body mass index (kg/m^2)	24.8 ± 3.1	24.6 ± 3.2	0.105	24.5 ± 3.2	24.1 ± 3.3	0.276	24.8±3.1	24.7±3.1	0.559
Hypertension	646 (69%)	900 (73%)	0.073	107 (71%)	279 (73%)	0.725	539 (68%)	621 (72%)	0.091
Diabetes mellitus	345 (37%)	581 (47%)	<0.001	60 (40%)	196 (51%)	0.020	285 (36%)	385 (45%)	<0.001
Heart failure	25 (3%)	38 (3%)	0.589	6 (4%)	19 (5%)	0.637	19 (2%)	19 (2%)	0.785
Dyslipidemia	617 (66%)	806 (65%)	0.644	91 (61%)	271 (71%)	0.025	526 (67%)	535 (62%)	0.054
Chronic kidney disease	52 (6%)	142 (11%)	<0.001	20 (13%)	71 (19%)	0.151	32 (4%)	71 (8%)	<0.001
Cerebrovascular accident	82 (9%)	139 (11%)	0.062	19 (13%)	51 (13%)	0.842	63 (8%)	88 (10%)	0.116
Left ventricular ejection fraction (%)	60.7 ± 11.9	59.6 ± 12.6	0.054	59.8 ± 12.2	57.3 ± 14.1	0.058	60.8±11.8	60.7±11.8	0.789
Preoperative hemoglobin (mg/dl)	13.4 ± 1.8	13.0 ± 2.1	<0.001	12.7 ± 2.1	12.5 ± 2.3	0.289	13.5±1.8	13.2±1.9	0.001
			<0.001			0.102			<0.001

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Table 1 (***Continued***)

Variable	Overall			Noncardiac surgery after DES implantation ≤12 months			Noncardiac surgery after DES implantation >12 months		
	Discontinuation of APT (n = 937)	Continuation of APT (n = 1,242)	p Value	Discontinuation of APT (n = 150)	Continuation of APT (n = 383)	p Value	Discontinuation of APT (n=787)	Continuation of APT (n=859)	p Value
Antiplatelet agents before surgery									
Aspirin only	521 (56%)	515 (42%)		29 (19%)	46 (12%)		492 (63%)	469 (55%)	
Clopidogrel only	75 (8%)	136 (11%)		5 (3%)	16 (4%)		70 (9%)	120 (14%)	
Aspirin plus clopidogrel	339 (36%)	574 (46%)		114 (76%)	308 (80%)		225 (29%)	266 (31%)	
Aspirin plus ticagrelor	2 (0%)	17 (1%)		2 (1%)	13 (3%)		0	4 (1%)	
Medication before surgery									
Warfarin	13 (1%)	29 (2%)	0.111	6 (4%)	8 (2%)	0.215	7 (1%)	21 (2%)	0.015
Beta-blocker	362 (39%)	486 (39%)	0.814	50 (33%)	133 (35%)	0.761	312 (40%)	353 (41%)	0.549
Calcium channel blocker	249 (27%)	334 (30%)	0.868	41 (27%)	109 (28%)	0.795	208 (26%)	225 (26%)	0.913
ACE inhibitor or ARB	317 (34%)	442 (36%)	0.394	48 (32%)	136 (36%)	0.444	269 (34%)	306 (36%)	0.540
Clinical diagnosis at DES implantation			0.300			0.059			0.786
Stable angina	547 (58%)	710 (57%)		93 (62%)	204 (53%)		454 (58%)	506 (59%)	
Unstable angina	224 (24%)	280 (23%)		34 (23%)	85 (22%)		190 (24%)	195 (23%)	
Acute myocardial infarction	166 (18%)	252 (20%)		23 (15%)	94 (25%)		143 (18%)	158 (18%)	
Time between DES and surgery (months)			<0.001			0.004			0.832
≤6	58 (6%)	201 (16%)		58 (39%)	201 (53%)				
>6, ≤12	92 (10%)	182 (15%)		92 (61%)	182 (48%)				
>12, ≤24	207 (22%)	222 (18%)					207 (26%)	222 (26%)	
>24	580 (62%)	637 (51%)					580 (74%)	637 (74%)	
Type of DES			<0.001			<0.001			0.014
First-generation	480 (51%)	488 (39%)		66 (44%)	88 (23%)		414 (53%)	400 (47%)	
Second-generation	457 (49%)	754 (61%)		84 (43%)	295 (77%)		373 (47%)	459 (53%)	
Total stent length (mm)			0.329			0.086			0.417
<20	288 (29%)	392 (32%)		43 (29%)	127 (33%)		225 (29%)	265 (31%)	
≥20, <40	520 (56%)	662 (53%)		92 (61%)	197 (51%)		428 (54%)	465 (54%)	
≥40	149 (16%)	188 (11%)		15 (10%)	59 (15%)		134 (17%)	129 (15%)	
No. of stents			0.629			0.446			0.474
1	772 (82%)	1039 (84%)		134 (89%)	324 (85%)		638 (81%)	715 (83%)	
2	144 (15%)	181 (15%)		15 (10%)	54 (14%)		129 (16%)	127 (15%)	
≥3	21 (2%)	22 (2%)		1 (1%)	5 (1%)		20 (3%)	17 (2%)	
Maximal stent diameter (mm)	3.11 ± 0.38	3.10 ± 0.39	0.724	3.1 ± 0.4	3.1 ± 0.4	0.457	3.1±0.4	3.1±0.4	0.488
Type of noncardiac surgery			0.067			0.250			0.278
Vascular/Orthopedic/Neurologic	245 (26%)	369 (30%)		42 (28%)	127 (33%)		203 (26%)	242 (28%)	
Thoracic/Abdominal/Urologic/Others	692 (74%)	873 (70%)		108 (72%)	256 (67%)		584 (74%)	617 (72%)	

Values are mean ± SD or n (%). Dyslipidemia was defined according to treatment criteria by the National Cholesterol Education Program Adult Treatment Panel III. ACE = angiotensin converting enzyme; APT = antiplatelet therapy; ARB = angiotensin II receptor blocker; DES = drug-eluting stent.

Table 2
Outcomes of discontinuation of antiplatelet therapy versus continuation of antiplatelet therapy

Variable	Discontinuation of APT	Continuation of APT	Unadjusted HR (95% CI)	p Value	IPTW-adjusted HR (95% CI)	p Value
Overall	(n = 937)	(n = 1242)				
Net adverse clinical event*	10 (1.1%)	22 (1.8%)	0.60 (0.28–1.27)	0.182	0.76 (0.38–1.52)	0.440
Composite of death, MI, and ST	9 (1.0%)	19 (1.5%)	0.63 (0.28–1.39)	0.248	0.80 (0.38–1.65)	0.542
All-cause of death	6 (0.6%)	11 (0.9%)	0.72 (0.23–1.95)	0.522	0.91 (0.35–2.36)	0.852
Myocardial infarction	4 (0.4%)	8 (0.6%)	0.66 (0.20–2.20)	0.500	0.87 (0.30–2.49)	0.793
Stent thrombosis	1 (0.1%)	1 (0.1%)	1.33 (0.08–21.18)	0.842	1.44 (0.13–15.90)	0.768
Major bleeding	2 (0.2%)	3 (0.2%)	0.88 (0.15–5.29)	0.892	1.18 (0.22–6.32)	0.851
NCS >1, ≤12 months after DES	(n = 150)	(n =383)				
Net adverse clinical event*	3 (2.0%)	7 (1.8%)	1.09 (0.28–4.17)	0.900	1.26 (0.36–4.38)	0.715
Composite of death, MI, and ST	3 (2.0%)	4 (1.0%)	1.92 (0.43–8.33)	0.394	2.34 (0.57–9.72)	0.241
All-cause of death	3 (2.0%)	3 (0.8%)	2.56 (0.52–12.50)	0.250	3.06 (0.66–14.13)	0.151
Myocardial infarction	1 (0.7%)	1 (0.3%)	2.56(0.16–49.98)	0.251	3.60 (0.25–52.28)	0.349
Stent thrombosis	1 (0.7%)	0	–	0.378	–	-
Major bleeding	1 (0.7%)	3 (0.8%)	0.85 (0.09–8.33)	0.890	0.99 (0.14–7.29)	0.991
NCS >12 months after DES	(n=787)	(n=859)				
Net adverse clinical event*	7 (0.9%)	15 (1.8%)	0.51 (0.21–1.25)	0.139	0.67 (0.30–1.52)	0.342
Composite of death, MI, and ST	6 (0.8%)	15 (1.8%)	0.43 (0.17–1.12)	0.085	0.59 (0.25–1.38)	0.224
All-cause of death	3 (0.4%)	8 (0.9%)	0.41 (0.11–1.54)	0.186	0.59 (0.17–2.03)	0.398
Myocardial infarction	3 (0.4%)	7 (0.8%)	0.47 (0.12–1.79)	0.268	0.60 (0.19–1.90)	0.383
Stent thrombosis	0	1 (0.1%)	–	–	–	–
Major bleeding	1 (0.1%)	0	–	–	–	–

Values are number (event rates). APT = antiplatelet therapy; CI = confidence interval; DES = drug-eluting stent; HR = hazard ratio; IPTW = inverse probability of treatment weighting; MI = myocardial infarction; NCS = noncardiac surgery; ST = stent thrombosis.

* Net adverse clinical event included a composite of death, myocardial infarction, stent thrombosis, and major bleeding.

before and after inverse probability weighting were provided in Supplemental Table 5.

Subgroup analyses for NACE are presented in Figure 3. There were significant interactions between perioperative APT and type of NCS (p-for-interaction = 0.023), indicating the discontinuation of APT is more favored as for vascular and/or orthopedic and/or neurologic NCS versus thoracic and/or abdominal and/or urologic and/or others NCS.

Discussion

The principal findings of the present study are that discontinuation of APT was not associated with higher NACEs at 30 days postsurgery compared with continuation of APT in patients undergoing elective NCS after DES implantation. Our findings persisted for NCSs >1, ≤12 months after DES, and for NCSs >12 months after DES. However, discontinuation of APT for >7 days was significantly associated with higher NACEs compared with discontinuation of APT ≤7 days.

Current guidelines recommend that aspirin be continued in most clinical situations as it provides benefits that outweigh the bleeding risk for patients with coronary stents and dual-APT. However, the evidence supporting this recommendation is weak.[2,15,16] These recommendations of maintenance of perioperative aspirin are based on previous findings that discontinuation of APT is one of the primary contributors to catastrophic stent thrombosis,[19,20] but there are no randomized trials particularly for patients with DES implantation. Meanwhile, in the present study, the proportion of patients who discontinued APT was 42%. Similarly, according to the Patterns of Non-Adherence to Anti-Platelet Regimens in Stented patients (PARIS) registry, over 40% of patients stopped both antiplatelet agents regardless of major or minor surgery, contrary to current guidelines.[21] Thus, in a real world clinical practice, the proportion of patients who discontinued APT before NCS may be greater than expected.

Similar to our findings, Hawn et al found no association between complete APT cessation and adverse cardiac events from a case-control analysis of 284 matched pairs.[6] Anwaruddin et al found that oral antiplatelet status at the time of surgery is not associated with adverse clinical outcomes from 606 surgeries of DES-treated patients.[10] Possible explanation could be found in the PARIS registry, in which a physician-guided dual-APT interruption of up to 14 days was not associated with subsequent thrombotic events.[22] Another explanation could be that, although types of major bleedings did not differ, minor bleedings in patients with continuation of APT could aggravate ischemic events. In the coronary revascularization demonstrating outcome study in the Kyoto (CREDO-Kyoto) registry, 2,398 patients underwent a surgical procedure within 3 years of stent implantation.[11] The 30-day major adverse cardiac event rates were 4.9% for dual-APT, 1.1% for single-APT, and 2.3% for no APT, and dual-APT tended to be associated with a higher risk for ischemic events, which appears to be paradoxical.

Contrary to these findings, Egholm et al reported from a population-based cohort study that absence of preoperative APT was associated with increased major adverse

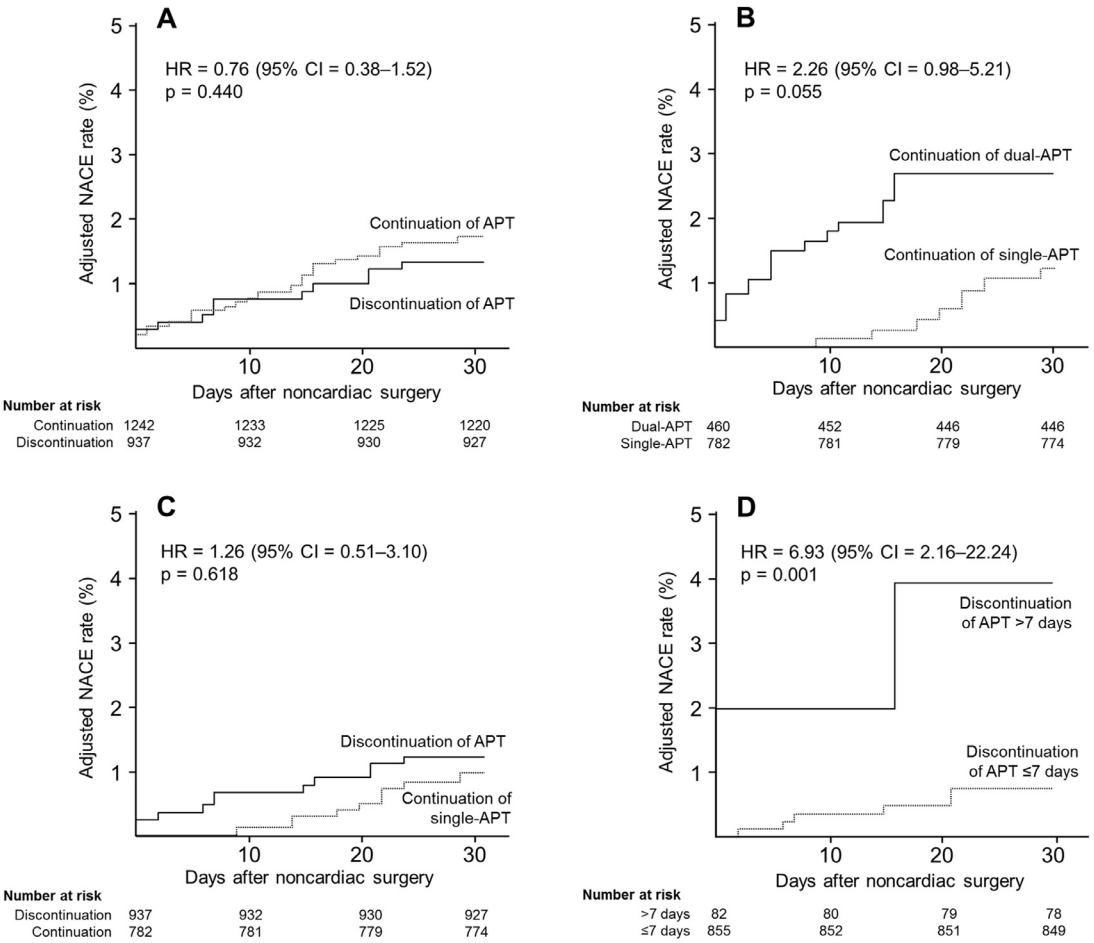

Figure 2. **Kaplan-Meier survival curves of adjusted net adverse clinical event according to the perioperative antiplatelet therapy strategy**. NACE included a composite of death, myocardial infarction, stent thrombosis, and major bleeding. Adjusted Kaplan-Meier survival curves were constructed using inverse probability of treatment weighting. APT = antiplatelet therapy; CI = confidence interval; HR = hazard ratio; NACE = net adverse clinical event; NCS = noncardiac surgery.

cardiac events.[13] However, their study included the NCS within the first year after DES implantation, also emergency surgery was underwent up to 49%. Similarly, Rossini et al reported that antiplatelet discontinuation increases the 30-day risk of major adverse cardiac events,[14] but their study included the patients whose timing from PCI to NCS was relatively shorter than our study. The proportion of NCS with PCI to NCS <180 days were 32%, but our proportion was only 12%. Also, they included the cardiac surgeries.

Although discontinuation of APT was not associated with a higher NACE than continuation of APT, we found that the duration of discontinuation was important. Consistent with our findings, Albaladejo et al reported on the interruption of antiplatelet treatment for >5 days preoperatively in patients with coronary stents who underwent NCS

Table 3
Outcomes of discontinuation of antiplatelet therapy versus continuation of single-antiplatelet therapy

Variable	Discontinuation of APT (n = 937)	Continuation of single-APT (n = 782)	Unadjusted HR (95% CI)	p Value	IPTW-adjusted HR (95% CI)	p Value
Net adverse clinical event	10 (1.1%)	8 (1.0%)	1.05 (0.41–2.65)	0.924	1.26 (0.51–3.10)	0.618
Composite of death, myocardial infarction, and stent thrombosis	9 (1.0%)	8 (1.0%)	0.94 (0.36–2.44)	0.900	1.12 (0.45–2.83)	0.805
All-cause of death	6 (0.6%)	4 (0.5%)	1.25 (0.35–4.44)	0.726	1.69 (0.46–6.21)	0.430
Myocardial infarction	4 (0.4%)	4 (0.5%)	0.84 (0.21–3.34)	0.800	0.91 (0.25–3.29)	0.888
Stent thrombosis	1 (0.1%)	0	–		–	–
Major bleeding	2 (0.2%)	0	–		–	–

Values are number (event rates). APT = antiplatelet therapy; CI = confidence interval; HR = hazard ratio; IPTW = inverse probability of treatment weighting.

Table 4
Outcomes of discontinuation of antiplatelet therapy >7 days versus discontinuation ≤7 days

Variable	Discontinuation of APT >7 days (n = 82)	Discontinuation of APT ≤7 days (n = 855)	Unadjusted HR (95% CI)	p Value	IPTW-Adjusted HR (95% CI)	p Value
Net adverse clinical event	4 (4.9%)	6 (0.7%)	7.10 (2.00–25.16)	0.002	6.93 (2.16–22.24)	0.001
Composite of death, myocardial infarction, and stent thrombosis	4 (4.9%)	5 (0.6%)	8.52 (2.29–31.73)	0.001	8.18 (2.43–27.47)	<0.001
All-cause of death	3 (3.7%)	3 (0.4%)	10.64 (2.15–52.71)	0.004	10.71 (2.46–46.58)	0.002
Myocardial infarction	2 (2.4%)	2 (0.2%)	10.63 (1.50–75.47)	0.018	9.15 (1.43–58.34)	0.019
Stent thrombosis	1 (1.2%)	0	–	–	–	–
Major bleeding	1 (1.2%)	1 (0.1%)	10.55 (0.66–168.68)	0.0957	10.56 (0.72–154.54)	0.085

Values are number (event rates). APT = antiplatelet therapy; CI = confidence interval; HR = hazard ratio; IPTW = inverse probability of treatment weighting.

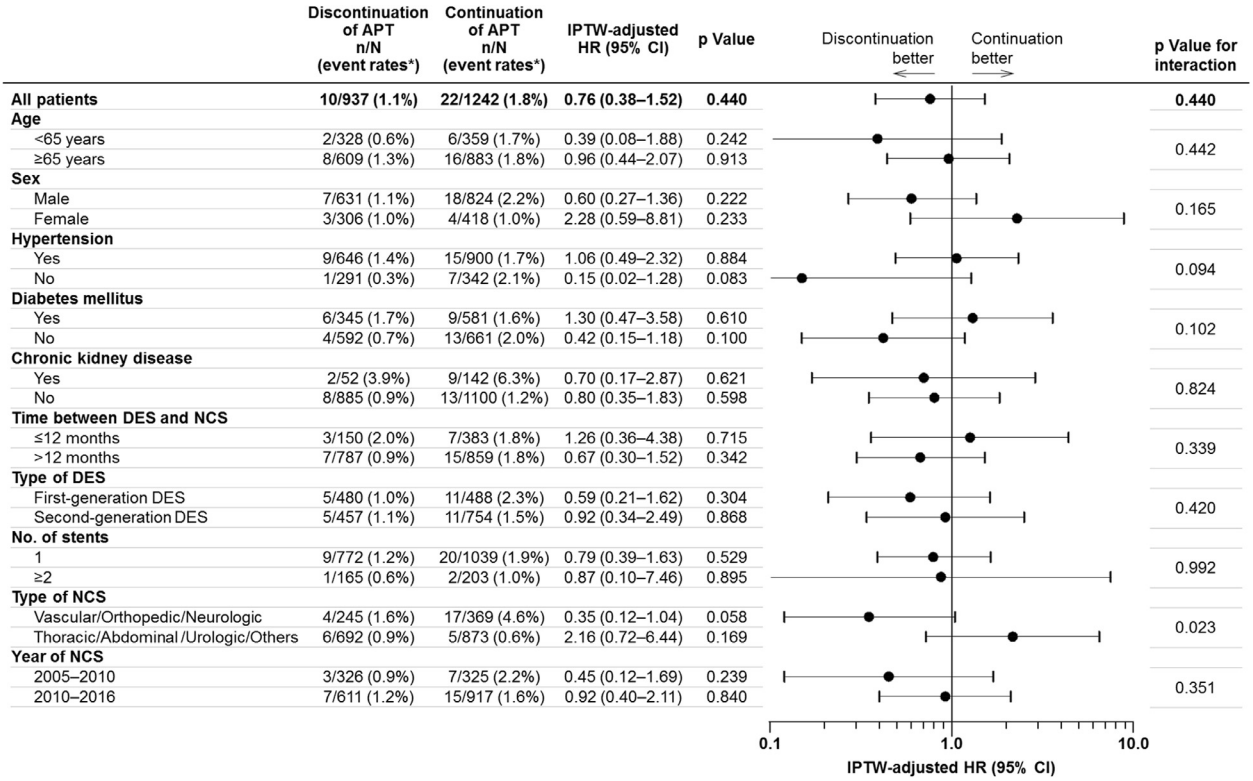

Figure 3. **Subgroup analyses of net adverse clinical events**. *Event rates and hazard ratios were calculated after adjustment with the use of IPTW. APT = antiplatelet therapy; CI = confidence interval; DES = drug-eluting stent; HR = hazard ratio; IPTW = inverse probability of treatment weighting; NCS = noncardiac surgery.

or another invasive procedure in a prospective observational study.[12] Although we could not confirm that patients who discontinued APT for >7 days did so due to physician-guided interruption, a possible explanation could be that these patients were noncompliant, which supports a previous study.[22]

Our study has some limitations. First, the number of patients included in the study is relatively small. However, we did analyze the largest number of DES-treated patients compared with previous studies. Second, the presence of residual confounding factors cannot be excluded, despite our inverse probability weighting adjustment. Large randomized trials to evaluate the role of perioperative APT in patients with coronary stents are needed. Third, this study lacks a non-PCI control group as used by other studies.[3,5] Fourth, our study did not include the assessment of peripheral artery disease which was shown to be the relevant parameters.[6]

Disclosures

The authors have no conflicts of interest to disclose.

Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.amjcard.2019.02.004.

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