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Aspirin Monotherapy vs No Antiplatelet Therapy in Stable Patients With Coronary Stents Undergoing Low-to-Intermediate Risk Noncardiac Surgery

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ABSTRACT

BACKGROUND Current guidelines recommend the perioperative continuation of aspirin in patients with coronary drug-eluting stents (DES) undergoing noncardiac surgery. However, supporting evidence is limited.

OBJECTIVES This study aimed to compare continuing aspirin monotherapy vs temporarily holding all antiplatelet therapy before noncardiac surgery in patients with previous DES implantation.

METHODS We randomly assigned patients who had received a DES >1 year previously and were undergoing elective noncardiac surgery either to continue aspirin or to discontinue all antiplatelet agents 5 days before noncardiac surgery. Antiplatelet therapy was recommended to be resumed no later than 48 hours after surgery, unless contraindicated. The primary outcome was a composite of death from any cause, myocardial infarction, stent thrombosis, or stroke between 5 days before and 30 days after noncardiac surgery.

RESULTS A total of 1,010 patients underwent randomization. Among 926 patients in the modified intention-to-treat population (462 patients in aspirin monotherapy group and 464 patients in the no-antiplatelet therapy group), the primary composite outcome occurred in 3 patients (0.6%) in the aspirin monotherapy group and 4 patients (0.9%) in the no antiplatelet group (difference, −0.2 percentage points; 95% CI: −1.3 to 0.9; $P > 0.99$). There was no stent thrombosis in either group. The incidence of major bleeding did not differ significantly between groups (6.5% vs 5.2%; $P = 0.39$), whereas minor bleeding was significantly more frequent in the aspirin group (14.9% vs 10.1%; $P = 0.027$).

CONCLUSIONS Among patients undergoing low-to-intermediate risk noncardiac surgery >1 year after stent implantation primarily with a DES, in the setting of lower-than-expected event rates, we failed to identify a significant difference between perioperative aspirin monotherapy and no antiplatelet therapy with respect to ischemic outcomes or major bleeding. (Perioperative Antiplatelet Therapy in Patients With Drug-eluting Stent Undergoing Noncardiac Surgery [ASSURE-DES]; NCT02797548) (JACC. 2024;84:2380–2389) © 2024 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

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Percutaneous coronary intervention (PCI) with drug-eluting stents (DES) has become the most common strategy for myocardial revascularization in patients with symptomatic ischemic heart disease.[1] Up to 20% of patients undergoing PCI with DES need surgical procedures within 2 years of coronary stent implantation, presenting a common yet challenging clinical scenario that demands balancing competing thrombotic and bleeding risks.[2,3]

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Current guidelines recommend postponing elective noncardiac surgery for at least 6 to 12 months after DES placement, continuing aspirin perioperatively to prevent stent thrombosis even beyond 1 year after PCI, and withholding $P2Y_{12}$ inhibitors for 5 to 7 days before the procedure.[4,5] These recommendations are based on observational studies that have shown a significant association between the premature discontinuation of antiplatelet therapy and fatal stent thrombosis, particularly after first-generation DES implantation.[6-8] Moreover, a secondary analysis from a randomized trial demonstrated that continued aspirin use reduced the risk of myocardial infarction in patients with previous PCI.[9] However, some observational studies found no association between the temporal discontinuation of antiplatelet therapy and perioperative adverse cardiac events, challenging these guideline recommendations.[3,10-14]

Given these conflicting findings, it remains uncertain whether aspirin monotherapy during the perioperative period reduces ischemic events or increases bleeding risk without clinical benefit. Therefore, we designed the ASSURE-DES (Aspirin in Patients With Drug-Eluting Stents Undergoing Noncardiac Surgery) trial to compare a strategy of continuing aspirin monotherapy vs temporarily (5 days) holding all antiplatelet therapy before noncardiac surgery in patients at least 1 year after PCI with DES.

ABBREVIATIONS AND ACRONYMS

DES = drug-eluting stent(s)

PCI = percutaneous coronary intervention

METHODS

STUDY DESIGN AND OVERSIGHT. The ASSURE DES trial was an investigator-initiated, multicenter, open-label, randomized, controlled trial conducted at 30 sites in 3 countries (Korea, India, and Türkiye). Details regarding the participating investigators and the organization of the trial are provided in Sections A and B of the Supplemental Appendix. The protocol (available on the *JACC* web site) was approved by the Institutional Review Board and ethics committee at each participating site. All patients provided written informed consent. All authors vouch for the accuracy and completeness of the data and for the fidelity of the trial to the protocol. The principal investigators had unrestricted access to the data, maintained the database, prepared the first draft of

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

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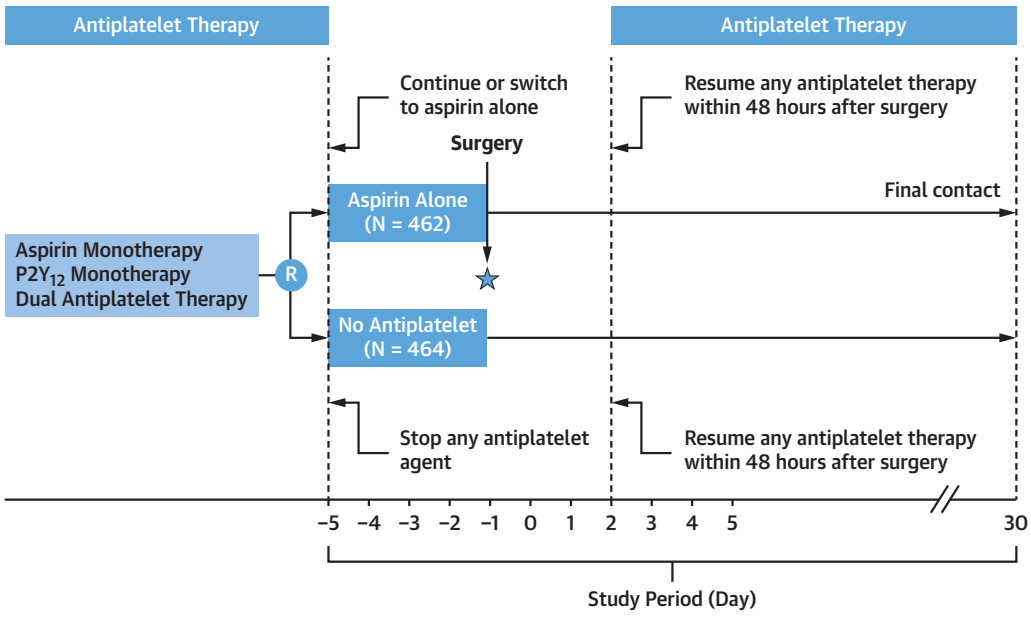
FIGURE 1 ASSURE DES Study Design



ASSURE DES = Aspirin in Patients With Drug-Eluting Stents Undergoing Noncardiac Surgery.

the manuscript, and made the decision to submit the manuscript for publication. In addition, an independent data and safety monitoring board approved the initial trial protocol and subsequent amendments and monitored patient safety periodically throughout the trial.

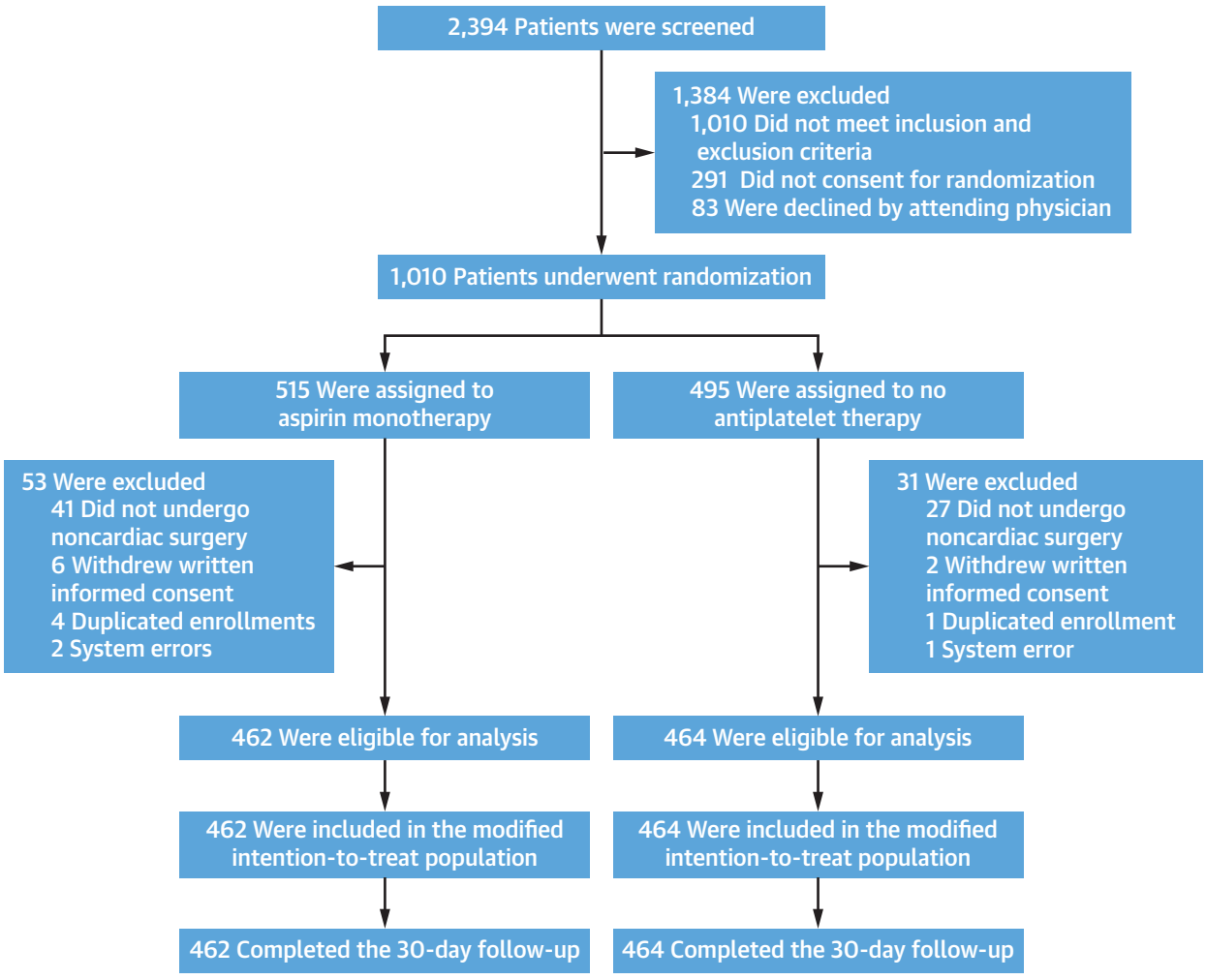
STUDY POPULATION. Eligible participants included adults who had undergone PCI with at least 1 DES >1 year earlier and were scheduled to undergo elective noncardiac surgery. Patients were excluded if they had an acute coronary syndrome or myocardial infarction within 1 month; severe left ventricular dysfunction (ejection fraction ≤30%) or valvular heart disease; intolerance to aspirin; a need for anticoagulation; emergent or cardiac surgery; or very high bleeding risk (eg, intracranial, spinal neurosurgery, or vitreoretinal eye surgery).[5] Full eligibility criteria are provided in Section C of the Supplemental Appendix.

PROCEDURES. Patients who were referred to cardiologists for preoperative cardiology consultation were screened. After providing written informed consent, eligible patients were randomly assigned in a 1:1 ratio using an interactive web-based system to receive either aspirin monotherapy or no antiplatelet therapy for 5 days before noncardiac surgery. Randomization was stratified according to participating center and surgical bleeding risk (Section D in the Supplemental Appendix) using randomly permuted blocks sizes of 4 or 6. The independent clinical events committee was masked to the group assignment.

In the aspirin monotherapy group, patients who were taking aspirin alone before randomization continued it at a dose of 100 mg/d throughout the perioperative period. For patients previously on a $P2Y_{12}$ inhibitor alone, the medication was switched to aspirin 5 days before surgery and continued during the perioperative period. For those on dual antiplatelet therapy, the $P2Y_{12}$ inhibitor was held 5 days before surgery while aspirin was continued. The $P2Y_{12}$ inhibitor was resumed as soon as possible after surgery at the discretion of the treating physicians.

In the no antiplatelet therapy group, all antiplatelet agents were discontinued 5 days before surgery and resumed as soon as possible after surgery, but no later than 48 hours postoperatively (**Figure 1**).[15] If significant bleeding occurred, antiplatelet therapy

FIGURE 2 Study Flow



could be discontinued at the discretion of the treating physician. Patients were followed clinically for 30 days after surgery through in-person visits or telephone contact.

OUTCOMES AND DEFINITIONS. The primary outcome was a composite of death from any cause, myocardial infarction, definite stent thrombosis, or stroke between 5 days before to 30 days after noncardiac surgery. Secondary outcomes included the individual components of the primary outcome and major or minor bleeding according to the TIMI definition. An independent clinical events committee, whose members were unaware of study-group assignments, adjudicated all primary and secondary outcome events. Myocardial injury after noncardiac surgery was defined as elevated postoperative cardiac troponin above the 99th percentile of the upper range limit in the absence of overt nonischemic causes among patients with a routine troponin test after noncardiac surgery.[16] Clinical outcomes were evaluated between 5 days before and 30 days after noncardiac surgery. The cardiovascular risk and bleeding risk of surgery were classified according to the European Society of Cardiology guideline[5] and the modified Johns Hopkins criteria,[17] respectively. The list and definitions of outcomes are provided in Sections D, E, F and G of the Supplemental Appendix.

STATISTICAL ANALYSIS. The null hypothesis was that there would be no between-group difference in the incidence of primary composite outcome at 30 days. Therefore, for the sample size calculation, the primary effect measure was the difference in the incidence of the primary composite outcome at

TABLE 1 Baseline Characteristics of the Patients

	Aspirin Monotherapy (n = 462)	No Antiplatelet Therapy (n = 464)
Age, y	68.0 ± 8.8	69.0 ± 9.0
Male	354 (76.6)	351 (75.6)
Geographic distribution		
South Korea	440 (95.2)	444 (95.7)
India	14 (3.0)	11 (2.4)
Türkiye	8 (1.7)	9 (1.9)
Body mass index, kg/m^2	25.0 ± 3.3	24.9 ± 3.5
Diabetes mellitus		
Any	193 (41.8)	221 (47.6)
Requiring insulin	32 (6.9)	34 (7.3)
Hypertension	402 (87.0)	389 (83.8)
Hyperlipidemia	423 (91.6)	416 (89.7)
Current smoker	65 (14.1)	62 (13.4)
Previous myocardial infarction	140 (30.3)	153 (33.0)
Previous congestive heart failure	10 (2.2)	16 (3.4)
Left ventricular ejection fraction, %	59.7 ± 8.5	59.0 ± 8.3
History of cerebrovascular disease	29 (6.3)	32 (6.9)
History of peripheral-artery disease	22 (4.8)	23 (5.0)
Atrial fibrillation or atrial flutter	16 (3.5)	14 (3.0)
Chronic renal insufficiency	38 (8.2)	55 (11.9)
Revised cardiac risk index[a]		
No risk factor	123 (26.6)	107 (23.1)
1 risk factor	200 (43.3)	208 (44.8)
2 risk factors	119 (25.8)	119 (25.6)
3 or more risk factors	20 (4.3)	30 (6.5)
Cardiovascular risk of surgery[b]		
High risk	55 (11.9)	50 (10.8)
Intermediate or low risk	407 (88.1)	414 (89.2)
Bleeding risk of surgery[b]		
High risk	57 (12.3)	54 (11.6)
Intermediate or low risk	405 (87.7)	410 (88.4)
Coronary stents		
Clinical presentation at index procedure		
Stable angina	186 (40.3)	188 (40.5)
Acute coronary syndrome	236 (51.1)	240 (51.7)
Unknown	40 (8.7)	36 (7.8)
Duration from stent implantation, y	5.1 (2.7-9.0)	5.4 (2.1-9.7)
First-generation drug-eluting stent[c]	51 (11.5)	55 (12.4)
Second or newer generation drug-eluting stent[c]	389 (88.0)	386 (86.9)
Left main or multivessel stenting	129 (27.9)	113 (24.4)
Stent number[c]	1.6 ± 0.8	1.6 ± 0.8
Stent diameter,[c] mm	3.1 ± 0.4	3.1 ± 0.4
Stent length,[c] mm	42.5 ± 25.0	40.5 ± 21.8
Antiplatelet therapy at randomization[d]		
Aspirin monotherapy	185 (40.0)	179 (38.6)
$P2Y_{12}$ inhibitor monotherapy	87 (18.8)	127 (27.4)
Dual antiplatelet therapy	178 (38.5)	141 (30.4)
No antiplatelet therapy	12 (2.6)	17 (3.7)

Continued on the next page

30 days between the 2 groups. On the basis of a prior available study,[9] we assumed that the incidence of the primary composite outcome at 30 days would be 6.0% for the aspirin monotherapy group and 11.5% for the no antiplatelet therapy group. We estimated that a sample size of 900 would provide the trial with 80% power, at a 2-sided significance level of 5%, to detect the difference in the incidence of primary composite outcome between the aspirin monotherapy group and the no antiplatelet therapy group. Details regarding the sample-size estimation and any amendments to it are provided in the Section G in the Supplemental Appendix.

All analyses were performed according to the modified intention-to-treat principle, which included all patients who underwent noncardiac surgery. Sensitivity analyses were performed in the as-treated (patients analyzed by actually received treatment) and per-protocol populations (patients analyzed as part of their assigned treatment group only if they actually received their assigned treatment). Continuous variables are reported as mean ± SD or median (Q1-Q3) and were compared using the Student's *t*-test or Wilcoxon rank-sum test. Categorical variables are presented as frequencies and percentages and were compared using the chi-square or Fisher exact test. The primary effect measure was the risk difference, with 95% CIs calculated by Wald methods. Regarding the primary outcome, the Fisher exact test was used to assess the superiority of aspirin monotherapy over no antiplatelet therapy. Analyses were performed using SAS software, version 9.4 (SAS Institute). A 2-sided *P* value <0.05 was considered to indicate statistical significance. The trial was registered (NCT02797548) and is now completed.

RESULTS

STUDY PATIENTS. From April 15, 2017, through March 5, 2024, a total of 1,010 patients at 30 participating centers in 3 countries were enrolled and randomly assigned before noncardiac surgery to aspirin monotherapy or no antiplatelet therapy. After excluding 84 patients (mainly because noncardiac surgery was not performed), 926 patients were included in the modified intention-to-treat primary analyses, of whom 462 patients were assigned to aspirin monotherapy and 464 patients were assigned to no antiplatelet therapy (**Figure 2**).

Baseline characteristics were similar in the 2 groups (**Table 1**). The mean age was 68.5 ± 9.0 years, 23.9% of patients were women, and 44.7% had diabetes. According to the revised cardiac risk index, 24.8% of patients had no risk factors, 44.1% had 1 risk factor, 25.7% had 2 risk factors, and 5.4% had 3 or more risk factors. The most common types of surgeries were abdominal (39.8%), orthopedic (23.3%), and urological or gynecological (18.7%) (Supplemental Table 1). Most surgeries were classified

as intermediate or low risk for both cardiovascular (88.7%) and bleeding (88.0%) events.[5,17] The median time from PCI with DES to noncardiac surgery was 5.1 years (Q1-Q3: 2.7-9.0 years); 87.5% of patients had second-generation or newer DES (median 4.4 years), and 11.4% received first-generation DES (median 13.9 years). At randomization, 39.3% of patients were on aspirin monotherapy, 23.1% on $P2Y_{12}$ inhibitor monotherapy, and 34.4% were on dual antiplatelet therapy. After surgery, the aspirin monotherapy group restarted antiplatelet therapy earlier (median 0 vs 2 days) and more frequently resumed dual antiplatelet therapy (36.8% vs 27.6%).

STUDY OUTCOMES. The 30-day follow-up was completed in all patients. The primary composite outcome occurred in 3 patients (0.6%) in the aspirin monotherapy group and 4 patients (0.9%) in the no antiplatelet therapy group (absolute difference, −0.2 percentage points; 95% CI: −1.3 to 0.9; $P > 0.99$) (Table 2). In the as-treated analysis, the rates of the primary composite outcome were 0.7% in the aspirin monotherapy group and 0.8% in the no antiplatelet therapy group ($P > 0.99$); in the per-protocol analysis, the rates of the primary composite outcome were 0.5% in the aspirin monotherapy group and 0.7% in the no antiplatelet therapy group ($P > 0.99$) (Supplemental Tables 2 to 4). Cardiac death caused by fatal myocardial infarction occurred in 2 patients (0.4%) in the aspirin monotherapy group only. Myocardial infarction occurred in 3 patients (0.6%) in the aspirin monotherapy group and in 3 patients (0.6%) in the no antiplatelet therapy group. Cardiac troponin was routinely evaluated in 283 patients. There was no difference regarding myocardial injury after noncardiac surgery (23.2% vs 20.0%; $P = 0.51$). There was no definite stent thrombosis in either group. The median time to the primary ischemic composite outcomes after noncardiac surgery was 1 day (Q1-Q3: 1-2 days).

Major bleeding occurred in 30 patients (6.5%) in the aspirin monotherapy group and 24 patients (5.2%) in the no antiplatelet therapy group ($P = 0.39$). Minor bleeding was more frequent in the aspirin monotherapy group (14.9% vs 10.1%; $P = 0.027$). Accordingly, the net adverse clinical events (including death from any cause, myocardial infarction, definite stent thrombosis, stroke, or major or minor bleeding) were more frequent in the aspirin monotherapy group (21.9% vs 16.2%; $P = 0.027$). The median time to major or minor bleeding after noncardiac surgery was 3 days (Q1-Q3: 2-5 days). Major bleeding according to the POISE-2 (Perioperative Ischemic Evaluation-2) trial definition (6.3% vs 5.2%; $P = 0.47$) and type 3, 5 bleeding according to the Bleeding Academic Research Consortium definition (14.0% vs 11.9%; $P = 0.34$) were also not different between groups.

Subgroup analyses according to the surgical and patient risk are presented in Supplemental Table 5. The results of these analyses were consistent with our primary findings.

TABLE 1 Continued

	Aspirin Monotherapy (n = 462)	No Antiplatelet Therapy (n = 464)
Antiplatelet therapy after surgery[e]		
Duration of antiplatelet discontinuation after surgery, d	0 (0-1)	2 (1-4)
Aspirin monotherapy	245 (53.0)	197 (42.5)
$P2Y_{12}$ inhibitor monotherapy	30 (6.5)	116 (25.0)
Dual antiplatelet therapy	170 (36.8)	128 (27.6)
No antiplatelet therapy	17 (1.8)	23 (5.0)

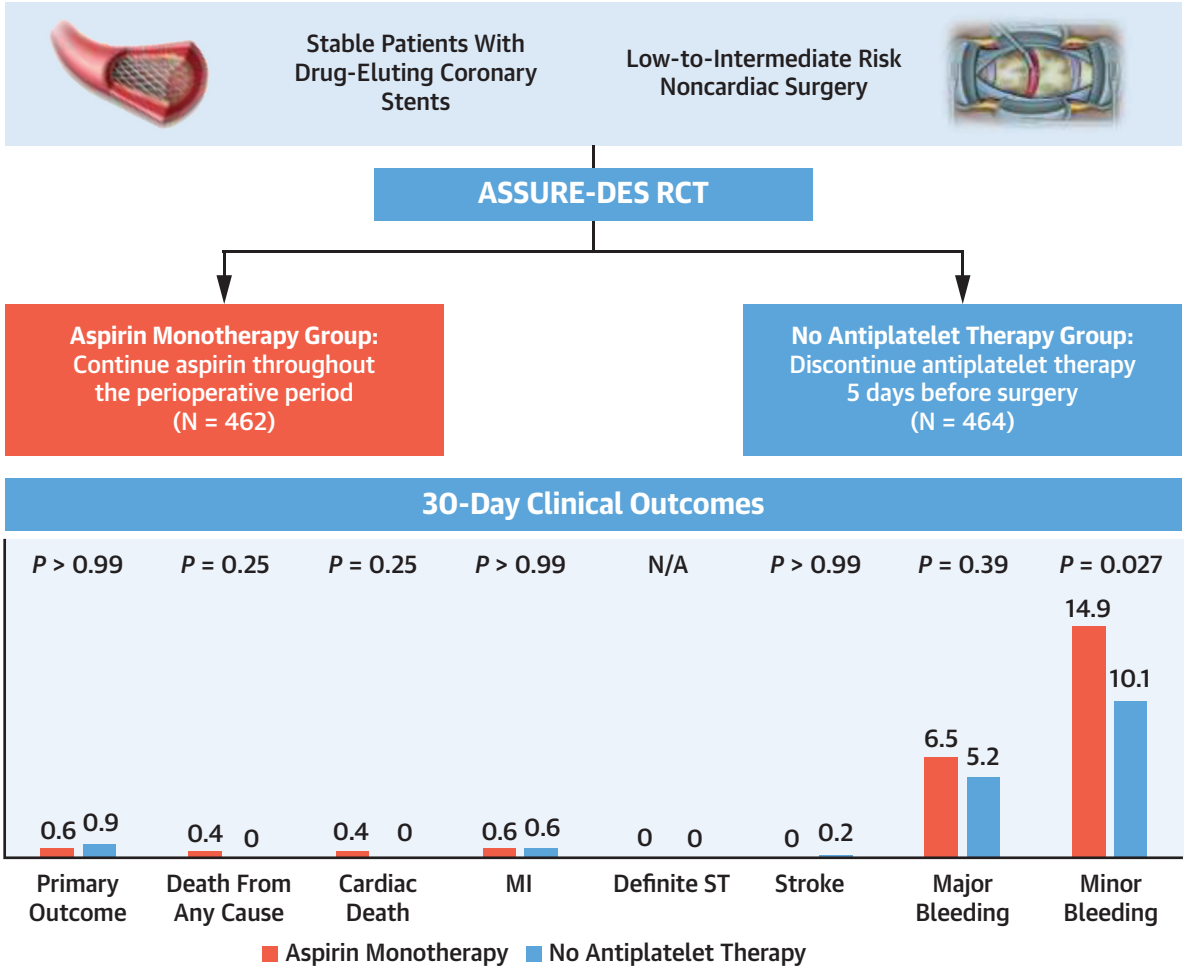
Values are mean ± SD, n (%), or median (Q1-Q3). [a]The revised cardiac risk index assesses the risk of cardiac complications in noncardiac surgery based on 6 factors including high-risk surgery, history of ischemic heart disease, history of congestive heart failure, history of cerebrovascular disease, preoperative treatment with insulin, and preoperative serum creatinine >2 mg/dL, with scores ranging from 0-6. [b]The cardiovascular risk and bleeding risk of surgery were classified according to the European society of cardiology guideline[5] and the modified Johns Hopkins criteria,[17] respectively. [c]Data for stent generation was available in 886 patients (5 of whom had bare-metal stents), and detailed stent size was available in 704 patients. [d]$P = 0.005$ for the comparison between the 2 groups. A total of 29 patients who had undergone coronary stent implantation an average of 8.0 ± 5.2 years before surgery were off antiplatelet therapy at baseline, likely caused by bleeding risk concerns. After screening, they resumed appropriate antiplatelet therapy before study enrollment. [e]$P < 0.001$ for the comparison between the 2 groups.

TABLE 2 Study Outcomes

	Aspirin Monotherapy (n = 462)	No Antiplatelet Therapy (n = 464)	*P* Value
Primary composite outcome[a]	3 (0.6)	4 (0.9)	>0.99
Secondary outcome			
Death from any cause	2 (0.4)	0 (0)	0.25
Cardiac death	2 (0.4)	0 (0)	0.25
Noncardiac death	0 (0)	0 (0)	–
Myocardial infarction	3 (0.6)	3 (0.6)	>0.99
Myocardial injury after noncardiac surgery[b]	32 (23.2)	29 (20.0)	0.51
Definite stent thrombosis[c]	0 (0)	0 (0)	–
Coronary revascularization	1 (0.2)	2 (0.4)	>0.99
Stroke	0 (0)	1 (0.2)	>0.99
Bleeding, any	99 (21.4)	71 (15.3)	0.016
Major[d]	30 (6.5)	24 (5.2)	0.39
Minor	69 (14.9)	47 (10.1)	0.027
Net adverse clinical event[e]	101 (21.9)	75 (16.2)	0.027

Values are n (%). [a]The primary composite outcome was the composite of death from any causes, myocardial infarction, stent thrombosis, or stroke at 30 days. [b]Myocardial injury after noncardiac surgery was defined as elevated postoperative cardiac troponin above the 99th percentile of the upper range limit in the absence of overt nonischemic causes among patients with routine troponin test after noncardiac surgery, and was assessed in 283 patients (138 patients in aspirin alone group and 145 patients in no antiplatelet group). [c]Stent thrombosis was defined according to Academic Research Consortium endpoint definitions. [d]Bleeding events were defined according to the TIMI definition. Major bleeding according to the POISE-2 (Perioperative Ischemic Evaluation-2) definition (6.3% vs 5.2%; $P = 0.47$), and type 3, 5 bleeding according to the Bleeding Academic Research Consortium definition (14.0% vs 11.9%; $P = 0.34$) were also not different between groups. [e]Net adverse clinical event was the composite of death from cardiac causes, myocardial infarction, stent thrombosis, stroke, major bleeding, or minor bleeding at 30 days.

CENTRAL ILLUSTRATION **Aspirin Monotherapy vs No Antiplatelet Therapy in Patients With Drug-Eluting Coronary Stents Undergoing Noncardiac Surgery**



Kang D-Y, et al. JACC. 2024;84(24):2380-2389.

ASSURE DES = Aspirin in Patients With Drug-Eluting Stents Undergoing Noncardiac Surgery; MI = myocardial infarction; RCT = randomized controlled trial; ST = stent thrombosis.

DISCUSSION

In this randomized trial involving patients undergoing noncardiac surgery >1 year after PCI with DES, we found no significant difference in the primary composite outcome of all-cause mortality, myocardial infarction, definite stent thrombosis, and stroke at 30 days between patients who perioperatively continued aspirin monotherapy and those who held all antiplatelet therapy starting 5 days before noncardiac surgery. There was also no significant difference in major bleeding, although minor bleeding was more frequent in the aspirin monotherapy group. Notably, no definite stent thrombosis occurred in either group (Central Illustration). Therefore, this study suggests that for patients undergoing

noncardiac surgery >1 year after PCI with contemporary DES, a more flexible approach to perioperative antiplatelet management, such as temporarily withholding all antiplatelet therapy, may be possible without compromising patient safety. However, the low event rate and predominance of low-to-intermediate risk surgeries enrolled in our study should be considered when interpreting these findings.

Current guidelines recommend perioperative continuation of aspirin in patients with coronary stents undergoing noncardiac surgery (Class I recommendation). This recommendation was initially based on expert opinion from observational studies with first-generation DES given the higher risk of stent thrombosis (Level of Evidence: C). It was recently updated following a post hoc analysis of the POISE-2 trial (Level of Evidence: B).[4,5] This analysis included 470 patients with previous PCI and found that perioperative continuation of aspirin compared with placebo was significantly associated with a lower incidence of death from any cause and nonfatal myocardial infarction.[9] However, this analysis was not prespecified, and the findings may not be directly applicable to our contemporary practice, because most stents (54.3%) in that study were bare-metal stents that differ significantly from current-generation DES in terms of thrombotic risk.[18,19]

However, several other studies have challenged current guideline recommendations. A large retrospective cohort study by Hawn et al[11] involving 41,989 operations in patients with coronary stents found that perioperative antiplatelet cessation was not significantly associated with adverse cardiac events. The PARIS (Patterns of Non-Adherence to Anti-Platelet Regimens in Stented Patients) registry prospectively evaluated the cessation pattern of dual antiplatelet therapy in 5,018 patients and found no significant increase in thrombotic events in patients with brief (<14 days) interruption of dual antiplatelet therapy for surgery (of those, all antiplatelet therapy was stopped in 70%), whereas most stent thrombosis occurred in patients on dual antiplatelet therapy.[12] The KOMATE (Korean Multicenter Angioplasty Team) registry, including 3,582 patients undergoing noncardiac surgery after second-generation DES, showed no significant impact of antiplatelet discontinuation on the risk of adverse perioperative events, except for prolonged (≥9 days) discontinuation. Notably, the incidence of stent thrombosis during the perioperative period was only 0.06% (2 events) in this registry.[14] Collectively, our trial along with previous studies strongly suggest that perioperative continuation of aspirin may not provide significant ischemic benefit to offset the potential bleeding risk in patients with contemporary DES.

Our results can be explained by several factors. The safety profile of contemporary-generation DES has significantly improved, with lower rates of stent thrombosis compared to first-generation DES,[20] as reflected in the recent shift towards a shorter duration of dual antiplatelet therapy.[21] Furthermore, our findings contribute to the ongoing reassessment of the thrombotic-bleeding risk balance in the perioperative setting, which continues to evolve with improvements in stent technology. For the small proportion of first-generation DES included in our study, >10 years had elapsed since implantation, well beyond the period of highest thrombotic risk. In the regions where this study was conducted, intracoronary imaging-guided PCI is commonly used, which may contribute to improved DES safety, although we did not collect specific data on its use in our study population.[22] In addition, our understanding of the risk profile of patients with coronary stents has improved over time, leading to various efforts to mitigate perioperative complications. Improved surgical techniques, less invasive surgeries, and enhanced perioperative care protocols likely contributed to our findings. The duration of antiplatelet discontinuation in our study (5 days) was shorter than the period associated with increased risk in previous observational studies, potentially minimizing the window of vulnerability to perioperative cardiac events while still providing time for platelet function recovery before surgery.[15] Last, the study population included mostly East-Asian patients, which may have a lower risk of ischemic events and higher risk of bleeding complications.

STUDY LIMITATIONS. First, although our study population—patients with DES who underwent noncardiac surgery—was exclusively considered high-risk for perioperative cardiovascular events, the observed event rates were remarkably lower than anticipated, potentially limiting our power to detect differences between groups. Second, our study design did not include routine measurement of perioperative cardiac enzymes for all patients, which may have led to an underestimation of myocardial infarction incidence. Unlike the POISE-2 trial, which implemented systematic cardiac biomarker assessments and likely captured more events,[9] our approach focused on clinically significant cases by testing only symptomatic patients. This methodological difference should be considered when interpreting our findings. Third, although the trial was open-label, outcome assessment was performed by an independent clinical

events committee that was masked to the group assignment. This was done to minimize selection bias and ensure objective evaluation of the primary and secondary outcomes. Fourth, low- to intermediate-risk surgeries were primarily included in the study, with very limited representation of high-risk procedures, such as vascular surgery. Consequently, our results should be cautiously applied in more complex, higher-risk surgical scenarios. Fifth, patients within the second year after stenting were underrepresented in our study. Finally, this study exclusively enrolled patients with stable conditions. Consequently, our findings cannot be applied to patients with acute coronary syndrome or other unstable conditions.

CONCLUSIONS

This randomized trial suggests that for patients undergoing noncardiac surgery >1 year after PCI primarily with a DES implantation, a strategy of continuing aspirin monotherapy did not significantly reduce ischemic events compared with temporarily (5 days) holding all antiplatelet therapy before noncardiac surgery. However, continuing aspirin was associated with a modest increase in minor bleeding. Given the lower-than-expected event rates and the underpowered nature of the study, these findings should be interpreted with caution. Further research with a large-scale, adequately powered study is needed to confirm these results, especially in higher-risk patients and surgeries.

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APPENDIX For an expanded Methods section and supplemental tables, please see the online version of this paper.