VIEWPOINT

Antiplatelet Therapy in Patients With Coronary Stents Undergoing Elective Noncardiac Surgery
Continue, Stop, or Something in Between?

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Surgeons, cardiologists, primary care physicians, and anesthesiologists frequently make decisions regarding antiplatelet management for patients undergoing elective surgery. Patients with recent coronary stent implantation can be particularly challenging as clinicians balance the cardiac risks of discontinuing therapy with the bleeding risks of continuing antiplatelet agents. More than 600 000 patients receive coronary stents annually in the United States, with up to 23% of these individuals requiring noncardiac surgery within 2 years.[1] Observational evidence suggests that patients who have undergone percutaneous coronary intervention with stent implantation are at increased risk of perioperative major adverse cardiac events (MACE) and that this risk is moderated by stent type (bare metal stent [BMS] vs drug-eluting stent [DES]), operative urgency, early discontinuation of antiplatelet therapy, and time from coronary intervention.[2-4]

Early studies in the pre-DES era showed the potential for major perioperative adverse outcomes in patients undergoing noncardiac surgery shortly after stent placement. In one retrospective study, 8 of 40 patients (20%) undergoing surgery within 6 weeks of stent placement died of either myocardial infarction or procedural hemorrhage.[2] After the advent of DES, subsequent cohort studies suggested that elevated thrombosis risk persisted for 6 weeks after BMS placement and up to 1 year following DES placement.[4] Second- and third-generation DES have lower thrombogenic risk,[5] and current American College of Cardiology (ACC) and American Heart Association (AHA) guidelines[6] recommend delaying noncardiac surgery until 30 days after BMS placement and ideally 6 months after DES placement unless clinical judgment indicates that the benefits exceed the risks for earlier (3-6 months after DES placement) surgery.

While the evidence surrounding timing of surgery appears robust, the role of antiplatelet agents in mitigating this risk is unclear. Continuing antiplatelet agents through the perioperative period may increase procedural bleeding, especially among patients receiving dual antiplatelet therapy (DAPT), whereas discontinuing antiplatelet agents may increase the risk of perioperative MACE, including acute stent thrombosis. The ACC/AHA guidelines[6] recommend that patients receiving DAPT undergoing elective surgery should continue aspirin through the perioperative period and restart the $P2Y_{12}$ inhibitor as soon as possible. The level of evidence is cited as expert opinion. A recent systematic review assessed the evidence regarding perioperative antiplatelet management to help guide clinicians with this common clinical conundrum.[7]

This review included a search of PubMed, Web of Science, and Scopus (through December 17, 2015) and identified 4608 possible citations. Of these, 13 studies addressed patients after percutaneous coronary intervention with stent placement who were undergoing elective noncardiac surgery, with MACE, bleeding outcomes, or both associated with perioperative antiplatelet management strategies (Table). None of the included studies were randomized clinical trials. Of the 13 observational studies, 2 were prospective, 10 were retrospective, and 1 had a case-control design. Most studies were small, with 9 of 13 studies including fewer than 150 patients, limiting power to detect differences in rare events. All studies included DES and 7 of 13 studies also included BMS. Multiple antiplatelet strategies were used both across and within a given study, including numerous permutations of preoperative (single antiplatelet therapy or DAPT) and perioperative (stop all, stop one, continue both, etc) options. Bridging—the temporary administration of an antithrombotic agent (eg, intravenous heparin) to avoid prolonged cessation of antiplatelet agents—was an additional layer of complexity in some studies; however, each study used a different antithrombotic agent and algorithm.

While these studies were too heterogeneous to statistically pool, qualitatively there was no signal of an association between antiplatelet strategy and MACE or bleeding rates. For example, 4 studies reported 0% MACE rates despite 3 different antiplatelet strategies including both continuing and discontinuing DAPT. Furthermore, among the studies that used DAPT preoperatively, the study with the highest MACE event rate (21.4%) continued aspirin, whereas the studies that discontinued both agents had lower MACE event rates (11.1% and 2.3%). Three studies reported 0% bleeding rates despite 3 different antiplatelet therapy strategies including continuing DAPT, continuing single antiplatelet therapy, and discontinuing all therapy, whereas the highest bleeding rate (14.8%) was reported in a study in which both agents were discontinued. In further assessment of these 13 studies by bridging strategy, timing of discontinuation of the antiplatelet agent, and type of surgery (eg, major vs minor, neurosurgery vs orthopedics), there was no evidence of a consistent pattern. Additional factors relevant to the cardiologist (eg, location of the stent, complexity of the percutaneous coronary intervention, acuity of presentation) and the surgeon (eg, reoperative site, intricacy of the operation) were not reported.

The one case-control study[1] included in the analysis reviewed 42 000 noncardiac operations within 2 years of coronary stent placement. It demonstrated an

Table. Summary of the Studies Included in the Systematic Review Including Preoperative and Perioperative Antiplatelet Strategies, Sample Size, and Event Rates

Preoperative Antiplatelet Strategy	Perioperative Antiplatelet Strategy	MACE			Bleeding		
		Studies, No.[a]	Patients, No.	Event Rate for Each Study, %	Studies, No.[a]	Patients, No.	Event Rate for Each Study, %
DAPT	Continue both	2	87	0, 0	3	108	0, 4.8, 9.5
	Continue one	1	14	21.4	1	14	0
	Stop both	2	115	2.3, 11.1	2	115	1.1, 14.8
DAPT or SAPT[b]	Continue	2	200	0.6, 4.8	2	200	9.5, 13.4
	Stop all	2	133	0, 2.7	1	22	0
Bridging[c]		5	271	Range, 0-7.8	5	271	Range, 0-22.3

Abbreviations: DAPT, dual antiplatelet therapy; MACE, major adverse cardiac events; SAPT, single antiplatelet therapy.

[a] Studies were included more than once if they calculated outcome rates for more than 1 antiplatelet strategy.

[b] Studies did not differentiate outcome rates for patients receiving DAPT vs SAPT preoperatively.

[c] Bridging studies used 1 or more of the preoperative and perioperative antiplatelet strategies listed above.

inverse relationship between time since stent implantation and risk of MACE and found that this risk returned to baseline at approximately 6 months, regardless of stent type. In a subanalysis of 284 patients with confirmed MACE matched 1:1 on multiple covariates including time from stent implantation and stent type, there was no difference in odds of MACE across 8 different preoperative and perioperative antiplatelet strategies.

Based on this available evidence, there is no clear association between antiplatelet strategy and rates of perioperative MACE and bleeding, even though physiological reasons would suggest that antiplatelet agents should be a factor in the risk of both. Any effect that does exist is likely small relative to other factors associated with MACE and bleeding, such as indication and urgency of operation, time since stent placement, invasiveness of the procedure, preoperative cardiac optimization, and underlying functional status. It is unlikely that observational studies will be able to control for these variables sufficiently to allow small effects to be detected or excluded.

Rather than continue to invest resources in observational studies, 1 or more adequately powered randomized clinical trials are needed. For example, to identify a reduction in MACE from 5% to 3%, a magnitude of difference frequently sought in cardiovascular research, approximately 1500 patients per treatment strategy would need to be studied—a sample much larger than any of the studies in the review. Conducting a study of such size would require substantial effort and administrative skill but should be within the capability of the cardiovascular community, which frequently publishes large randomized trials. Such trials would also provide the opportunity to collect data on the large number of factors—other than antiplatelet management—that potentially influence MACE and bleeding risk, such as location of the stent and details about the surgical procedure. In the meantime, the decision about perioperative antiplatelet management should remain individualized, made by an informed decision-making process involving the surgeon, anesthesiologist, cardiologist, and patient.

ARTICLE INFORMATION

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