CHEST

Original Research

CARDIOVASCULAR DISEASE

Perioperative Management of Antiplatelet Therapy in Patients With a Coronary Stent Who Need Noncardiac Surgery

A Systematic Review of Clinical Practice Guidelines

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Background: **It is unclear how to appropriately manage discontinuation and resumption of antiplatelet therapy in patients with coronary stents who need noncardiac surgery. We undertook a systematic review of the literature to identify practice guideline statements regarding antiplatelet therapy in patients with coronary stents undergoing noncardiac surgery.**

Methods: **We used six search strategies to identify practice guideline statements that comment on perioperative antiplatelet management for patients with coronary stents undergoing noncardiac surgery. Two independent reviewers assessed study eligibility, abstracted data, and completed quality assessment.**

Results: **We identified 11 practice guidelines that met the eligibility criteria; these were included in the review. These guidelines advised that elective noncardiac surgery be delayed for at least 4 weeks after bare-metal stent implantation and at least 6 months after drug-eluting stent implantation. For elective surgery, all guidelines advised continuing acetylsalicylic acid (ASA) therapy whenever possible. If interruption of antiplatelet therapy was required, four guidelines advised to discontinue ASA/clopidogrel at least 5 days before surgery, while two guidelines advised to discontinue 7 to 10 days before surgery. Five guidelines provided varying guidance for the use of perioperative bridging during antiplatelet therapy interruption.**

Conclusions: **Most current recommendations are based on expert opinion. This review highlights the need for well-designed prospective studies to identify optimal management strategies in patients with coronary stents who are on antiplatelet therapy and who need noncardiac surgery.**

CHEST 2013; 144(6):1848–1856

Abbreviations: AGREE = Appraisal of Guidelines Research and Evaluation; ASA = acetylsalicylic acid; BMS = bare-metal stent; DAPT = dual antiplatelet therapy; DES = drug-eluting stent; MACE = major adverse cardiovascular event; ST = stent thrombosis

Major perioperative cardiovascular complications such as nonfatal myocardial infarction, nonfatal stroke, and death occur in nearly 10 million patients annually.[1] This number is expected to rise due to the increase in noncardiac surgery and other procedures performed in an aging population. The perioperative management of patients with coronary artery stents is particularly challenging and is becoming more common, as 900,000 patients receive coronary stents in the United States annually.[2] Coronary stents consist of bare-metal stents (BMSs) or, in the majority of cases in the United States, drug-eluting stents (DESs). After stent implantation, it is recommended that patients receive 6 weeks to 12 months of dual antiplatelet therapy (DAPT),[3,4] typically consisting of acetylsalicylic acid (ASA) combined with clopidogrel, although DAPT often is continued beyond this time frame. Within 1 year of stent implantation, 4% to 5% (36,000-45,000 patients) of such patients will require surgery, a number that rises to 11% (99,000 patients) within 2 years of stenting.[5] It is anticipated that a much higher number of stented patients will require nonsurgical procedures such as colonoscopy.

There are no established management strategies for patients with coronary stents who are receiving DAPT and require elective surgery. Clinicians balance

the perceived risk for major adverse cardiovascular events (MACEs) and stent thrombosis (ST) associated with perioperative antiplatelet drug interruption against the risk of bleeding associated with drug continuation. Patients with coronary stents have an 8% to 10% risk of developing MACE and ST after elective noncardiac surgery,[6,7] which exceeds the 1% to 5% risk for MACE in nonstented patients having noncardiac surgery.[8] Given that fatality from ST ranges from 40% to 60%, this represents a significant clinical problem.[9,10] Patients are at highest risk for ST during the time between stent implantation and re-endothelialization at the stent site. This process takes 4 to 6 weeks in patients with a BMS and 6 to 12 months in patients with a DES.[11] Premature withdrawal of DAPT is the strongest predictor of ST, with the majority of drug withdrawals occurring in the perioperative setting.[12] The risk for MACE and ST diminishes as the interval between stent implantation and surgery increases, irrespective of the stent type, but remains at 5% to 10% if surgery is done > 2 years after stenting.[13,14]

There are few well-designed studies to inform perioperative management of stented patients who need elective surgery, specifically about when to interrupt and resume DAPT and whether one or both antiplatelet drugs should be continued or stopped. Thus, although one observational study found that stopping both antiplatelet drugs > 5 days before surgery conferred a 2.1-fold increased risk for MACE, an optimal management was not identified.[15] Similarly, the risk of bleeding if antiplatelet therapy is continued perioperatively is uncertain,[15] and although continuing ASA appears to increase the risk for major bleeding (from 1% to 2%), this estimate is imprecise as the definition of bleeding was not standardized.[16]

Given the paucity of well-designed studies to inform practice, clinicians may rely on practice guidelines to assist with decisions regarding perioperative antiplatelet management in patients with coronary stents who need noncardiac surgery. While such guidelines are available, they appear to vary according to methodological approaches and recommendations. We undertook a systematic review of the literature aiming to evaluate and synthesize guideline statements regarding perioperative antiplatelet therapy focusing on the following clinical questions:

1. When should elective noncardiac surgery be done in patients with a coronary stent?
2. Which antiplatelet agents should be stopped or continued around the time of surgery?
3. When should antiplatelet therapy be stopped and resumed before and after surgery?
4. Is bridging with an anticoagulant or antiplatelet agent needed around the time of surgery?

Materials and Methods

Study Eligibility Criteria

We included clinical practice guidelines that comment on perioperative antiplatelet management strategies for patients with coronary stents who are having noncardiac surgery. Studies were eligible regardless of their language, publication status, primary objective, or size and scope of the practice guideline group. We excluded studies that were not deemed to be guideline statements, duplicate publications, copies or summaries of previous guidelines, and guidelines that did not provide recommendations or statements pertaining to any of the aforementioned clinical questions.

Study Identification and Search Strategy

We used the following strategies to identify eligible studies: electronic search of databases, including the National Guideline Clearinghouse website (http://www.guideline.gov, accessed January 2013), MEDLINE (1946 to January, week 1, 2013), EMBASE (1974 to 2012, week 52), AMED (1985 to December 2012), and Cochrane Library (until December 2012); consultation with experts in perioperative medicine; review of reference lists from retrieved articles fulfilling eligibility criteria; use of the "see related articles" for key publications in PubMed (until January 2013); and search of SciSearch (until January 2013) for publications that cited key publications.

Study Selection

Search results were merged using reference management software (RefWorks), and duplicate records were removed. All titles and abstracts of identified articles were independently screened by two authors (S. D.-K., M. G.). If either reviewer considered that a citation contained a guideline of interest, the citation was selected for full review. After retrieving the full text of citations selected for full review, the same two authors independently assessed eligibility. A κ statistic was used to quantify interobserver agreement. Any disagreements were resolved by discussion among the two reviewers. An independent third author (M. M.) resolved any outstanding disagreements. If there were questions regarding the methods of a reviewed article, we contacted the study authors for clarification.

The eligibility criteria for each article were assessed in a predetermined order and the first criterion not met was used as the reason for exclusion. The order was as follows: guideline statements, involved patients having noncardiac surgery, comments specifically

Manuscript received February 25, 2013; revision accepted July 2, 2013.
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Funding/Support: Support for this work was provided to Dr Douketis as the recipient of the CHEST Foundation GlaxoSmithKline Distinguished Scholar Award in Thrombosis.
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DOI: 10.1378/chest.13-0459