JAMA Clinical Guidelines Synopsis

Perioperative Management of Antithrombotic Therapy

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GUIDELINE TITLE Perioperative Management of Antithrombotic Therapy: An American College of Chest Physicians Clinical Practice Guideline

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DEVELOPER AND FUNDING SOURCE American College of Chest Physicians

TARGET POPULATION Patients taking oral anticoagulation or antiplatelet therapy who are undergoing an elective surgery or procedure

SELECTED RECOMMENDATIONS

- For patients requiring aspirin therapy who are undergoing an elective noncardiac surgery, continuing aspirin through the surgery is suggested (conditional recommendation; moderate certainty of evidence [COE]).
- For patients with atrial fibrillation taking vitamin K antagonists (VKAs) who are undergoing an elective surgery or procedure with low to moderate risk of thromboembolism, temporary use of therapeutic heparin doses during interruption of VKA (heparin bridging) is not recommended (strong recommendation; moderate COE).
- For patients with a mechanical heart valve with low to moderate risk of thromboembolism who require VKA interruption for an elective surgery or procedure, heparin bridging is not suggested (conditional recommendation; very low COE).
- For patients receiving a direct oral anticoagulant (DOAC) who will be undergoing an elective surgery or procedure, discontinuing DOAC therapy is suggested with the timing dependent on the specific DOAC and the bleeding risk of the procedure (conditional recommendation; very low COE).

Summary of the Clinical Problem

Among patients taking therapeutic anticoagulation, the competing thrombotic and bleeding risks lead to complex perioperative decision-making. These guidelines[1] aim to optimize the perioperative management of antithrombotic medications.

The guideline defines surgeries as interventions requiring anesthesia with or without hospitalization, and procedures as minor interventions that do not typically require hospitalization (such as dental, dermatologic, ophthalmologic, pacemaker/internal cardiac defibrillator implantation, and gastrointestinal endoscopy procedures). The perioperative period begins 1 week prior to the intervention and ends 4 weeks later. Patients at high risk of perioperative thromboembolism have greater than a 10% yearly risk of arterial embolism or greater than a 10% monthly risk of venous thromboembolism (VTE); moderate risk is 4% to 10% yearly for arterial embolism or 4% to 10% monthly for VTE; and low risk is less than 4% yearly for arterial embolism and less than 2% monthly for VTE. Bleeding risk is considered high when the intervention is associated with a 2% or greater risk of major bleeding up to 30 days after the intervention, moderate risk implies less than 2% probability, and minimal risk approximates 0%.

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Characteristics of the Guideline Source

The guideline panel included internists, surgeons, intensivists, pharmacists, cardiologists, thrombosis specialists, and methodology experts (**Table**). The literature was searched from December 2011 to July 2021. The GRADE approach was used to assess COE and classify it as high, moderate, low, or very low, with final recommendations stated as either strong (recommended) or conditional (suggested).

Evidence Base

Of 44 recommendations, 2 were rated as strong with moderate COE, 1 was conditional with moderate COE, and 41 were conditional with low or very low COE.

For patients taking aspirin, continuation for elective noncardiac surgery is suggested. In a randomized clinical trial (RCT) of 17 444 patients undergoing acute hip fracture repair or elective hip or knee replacement, patients were randomized to aspirin, 160 mg/d, vs placebo, started at time of trial entry (82% of patients starting preoperatively) and continued postoperatively for 35 days. Patients taking aspirin had decreased risk of VTE vs placebo (1.5% vs 2.2%; $P < .001$), increased risk of major bleeding (2.5% vs 1.8%; $P < .001$) and myocardial infarction (1.3% vs 1.0%; $P = .04$), and similar risk of stroke (0.7% vs 0.6%; $P = .58$).[2] Another RCT included 10 010 patients with increased risk of a vascular complication (including history of coronary artery disease, peripheral arterial disease, or stroke, or multiple risk factors for vascular disease) who underwent noncardiac surgery. There was no difference in rates of death or nonfatal myocardial

Table. Guideline Rating[a]

Standard	Rating
Establishing transparency	Good
Management of conflict of interest in the guideline development group	Good
Guideline development group composition	Good
Clinical practice guideline–systematic review intersection	Fair
Establishing evidence foundations and rating strength for each of the guideline recommendations	Fair
Articulation of recommendations	Good
External review	Poor
Updating	Fair
Implementation issues	Fair

[a] Cifu AS, Davis AM, Livingston EH. Introducing JAMA Clinical Guidelines Synopsis. *JAMA*. 2014;312(12):1208-1209. doi:10.1001/jama.2014.12712

infarction among those who initiated or continued aspirin preoperatively vs those randomized to placebo (7.0% vs 7.1%; $P = .92$).[3] However, individuals taking aspirin had a higher 30-day bleeding risk vs placebo (4.6% vs 3.8%; $P = .04$).[3] There are no prospective studies to guide perioperative management of patients undergoing noncardiac surgery who are taking other antiplatelet agents such as clopidogrel, prasugrel, or ticagrelor. For those taking aspirin plus a P2Y12 inhibitor and undergoing coronary artery bypass graft surgery, continuing aspirin but withholding clopidogrel (5 days), prasugrel (7 days), or ticagrelor (3-5 days) is suggested based on low COE.[1]

The guidelines issued a strong recommendation against temporary use of therapeutic heparin doses during interruption of VKA (heparin bridging) for elective surgeries or procedures in patients with atrial fibrillation and low to moderate thrombotic risk (CHA_2DS_2-VASc score ≤6 or $CHADS_2$ score ≤4). An RCT of 1884 patients showed that forgoing heparin bridging was noninferior to bridging for preventing arterial embolism (0.4% vs 0.3%; mean between-group difference, 0.1%; 95% CI, −0.6% to 0.8%)[4] and was associated with less major bleeding (no bridging: 1.3%; bridging: 3.2%; $P = .005$).[4]

The suggestion that patients receiving VKA for mechanical heart valves do not require postoperative heparin bridging for low to moderate thrombotic risk is based on subgroup analyses from RCTs and observational data. In an RCT of 1471 VKA-treated patients, VKA was discontinued 5 days prior to the intervention and all patients received preoperative dalteparin. Postoperatively, all patients resumed warfarin and received either postoperative bridging with dalteparin or placebo until they had a therapeutic international normalized ratio. Among the 21% of participants with a mechanical heart valve, no significant difference was observed after 12 weeks in major thromboembolism (0% vs 0.67%; risk difference, 0.7%; 95% CI, −0.6% to 2.0%) or bleeding (1.96% vs 0.67%; risk difference, −1.3%; 95% CI, −3.8% to 1.3%).[5] In a meta-analysis of 8 observational studies of heparin bridging vs no bridging in 5184 patients undergoing an intervention and taking VKA therapy, 24% of whom had a mechanical heart valve, there was no association with arterial embolism risk (odds ratio, 0.8; 95% CI, 0.36-1.95), but heparin bridging was associated with increased risk of major bleeding (OR, 3.6; 95% CI, 1.52-8.5).[6]

Discontinuation of dabigatran for 1 to 4 days before an elective surgery or procedure or 1 to 2 days prior for apixaban, edoxaban, or rivaroxaban is suggested, with the specific timing dependent on the bleeding risk of the procedure. Patients with atrial fibrillation taking dabigatran had low 30-day arterial embolism rates (0.2%; 95% CI, 0%-0.5%) and low 30-day major bleeding events (1.8%; 95% CI, 0.7%-3%) after 24-hour interruption prior to their intervention for low-bleeding-risk procedures and 48-hour interruption for high-bleeding-risk interventions.[7] Another prospective cohort study of 3007 patients with atrial fibrillation taking apixaban, dabigatran, or rivaroxaban who were undergoing an elective surgery or procedure evaluated DOAC interruptions without use of heparin bridging beginning 1 day prior through 1 day after the intervention (for low- to moderate-bleeding-risk interventions) or 2 days prior through 2 to 3 days after the intervention (for high-bleeding-risk interventions). DOAC interruptions were associated with low 30-day rates of arterial embolism (0.2%-0.5%) and major bleeding (1.0%-1.7%).[8]

Benefits and Harms

These guidelines primarily offer benefit by attempting to standardize perioperative antithrombotic management, thereby reducing clinician-level variability in practice. Stratification of the recommendations around an individual's thrombotic risk taken with the procedural bleeding risk is likely to minimize perioperative complications.

Discussion

There is a paucity of prospective evidence to inform many decisions around perioperative management. Even when prospective evidence is available, its generalizability is limited. For example, nearly all data regarding perioperative DOAC management are extrapolated from patients with atrial fibrillation, despite the increasing use of DOACs for management of VTE, peripheral arterial disease, and stable coronary disease.[1]

Areas in Need of Future Study/Ongoing Research

Little evidence is available to guide management of patients with severe chronic kidney disease, particularly those with creatinine clearance of less than 30 mL/min. Identifying optimal patient- and system-level implementation strategies to standardize anticoagulation management across a variety of clinical settings is also needed.

ARTICLE INFORMATION

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