PERIOPERATIVE MANAGEMENT OF ANTIPLATELET THERAPY



OBJECTIVE:

To provide guidance to clinicians, based on the Canadian Cardiovascular Society recommendations, for the perioperative management of patients on antiplatelet therapy who require non-cardiac or cardiac surgery.

BACKGROUND:

Antiplatelet drugs are commonly used in the primary and secondary prevention of cardiovascular disease. Patients receiving antiplatelet therapy have a broad range of cardiovascular risk depending on the clinical indication for treatment.

With over 200 million noncardiac surgical procedures performed worldwide each year, clinicians face unique challenges regarding the perioperative management of patients with coronary artery disease who are receiving acetylsalicylic acid (ASA) alone; clopidogrel alone; ASA and clopidogrel; ASA and dipyridamole; or ASA combined with prasugrel or ticagrelor. Clinicians must balance the risks of major adverse cardiovascular events associated with interrupting these therapies against the risk of bleeding from continuing these therapies in the perioperative period. Additionally, other factors including the pharmacokinetic actions of antiplatelet drugs and the optimal timing of surgery in patients with coronary stenting must be considered. The latter group of patients requires special consideration due to the increased risks and significant mortality of stent thrombosis.

RISK STRATIFICATION FOR PERIOPERATIVE THROMBOSIS AND BLEEDING

Risk stratification for thrombosis and bleeding is largely empiric in patients who are receiving antiplatelet therapy. Patients considered at highest risk for cardiovascular events in the perioperative period include those with recently implanted bare metal stents (BMS) or drug-eluting stents (DES), recent myocardial infarction (MI), those with carotid ulcerating plaque and stroke or aortic ulcerating plaque and systemic embolism. Patients at low risk for perioperative cardiovascular events are those taking antiplatelet therapy for primary prevention of MI or stroke (although this is rarely indicated). Clinicians must balance these risks against the associated risks of perioperative bleeding (listed in Table 1).

DIAGNOSTIC TESTING, ARTHROCENTESIS, AND MINOR DENTAL, SKIN AND EYE PROCEDURES

Patients undergoing arthrocentesis, minor dental (extraction, root canal), eye (cataract) or skin (biopsy, skin cancer excision) procedures, as well as low bleeding risk diagnostic procedures, can continue ASA without interruption. Less is known about the safety of continuing P2Y12 inhibitors (clopidogrel, ticagrelor, prasugrel) around minor procedures when taken as monotherapy. It is reasonable to discontinue them for a short period (3-4 days) before the procedure. If patients are also taking ASA (dual antiplatelet therapy), the P2Y12 should be discontinued for 5-7 days prior.

Patients having a diagnostic test associated with a higher risk for bleeding should be managed as for higher risk procedures, as outlined below.

MANAGEMENT OF PATIENTS WITHOUT CORONARY STENTS UNDERGOING ELECTIVE OR NON-URGENT NONCARDIAC SURGERY

The Perioperative Ischemic Evaluation (POISE) 2 trial is the only randomized trial in noncardiac surgery to assess perioperative antiplatelet drug management. It demonstrated that ASA did not have an effect on the incidence of major adverse cardiovascular events or mortality but increased the risk of major bleeding. Only 4% of patients in this study had a coronary stent and it excluded patients who underwent carotid endarterectomy, received a BMS in the 6 weeks before surgery, or a DES in the 12 months before surgery.

Initiating ASA before surgery to reduce perioperative cardiovascular events is not recommended.

ASA should be discontinued 7 to 10 days prior to elective or non-urgent non-cardiac surgery except in patients undergoing carotid endarterectomy or with recent coronary artery stenting (see below for approach).

In patients with an indication for chronic ASA, this medication should be resumed when the risk of bleeding related to surgery has passed, usually between 8-10 days after major noncardiac surgery.

MANAGEMENT OF PATIENTS WITH CORONARY STENTS UNDERGOING ELECTIVE OR NON-URGENT NONCARDIAC SURGERY

A sub-study of the POISE-2 trial involving 470 patients with previous PCI and cardiac stents revealed that for every 1000 patients with prior PCI, perioperative aspirin will prevent 59 myocardial infarctions but cause 8 major bleeds. It is, therefore, viewed that in patients with prior PCI undergoing noncardiac surgery, perioperative aspirin may be more likely to benefit than harm patients.

Clinicians must consider the timing of surgery and perioperative dual antiplatelet (DAPT) management in patients being treated with DAPT after a percutaneous coronary intervention (PCI) with a BMS or DES.

	Timing of Non-cardiac Surgery	Perioperative Antiplatelet Management
PCI Patients with a Bare Metal Stent	Recommended to delay surgery for at least 1 month after PCI	ASA should be continued perioperatively. Clopidogrel and ticagrelor should be withheld 5-7 days preoperatively, and prasugrel 7-10 days preoperatively P2Y12 inhibitor should be restarted as soon as it is deemed safe by the surgeon
PCI Patients with a Drug Eluting Stent	Recommended to delay surgery for at least 3 months after PCI. If semi- urgent surgery is required, surgery should be delayed at least 1 month after PCI with a DES.	ASA should be continued perioperatively. Clopidogrel and ticagrelor should be withheld 5-7 days preoperatively, and prasugrel 7-10 days preoperatively P2Y12 inhibitor should be restarted as soon as it is deemed safe by the surgeon

MANAGEMENT OF PATIENTS REQUIRING ELECTIVE OR SEMI-URGENT CABG AFTER ACUTE CORONARY SYNDROME (ACS)

Coronary artery bypass grafting is associated with a high risk of bleeding with potentially significant consequences (i.e. cardiac tamponade, death). An interdisciplinary assessment of the risks of coronary thrombotic complications and risk of perioperative bleeding should be performed with the surgeon, interventional cardiologist, attending physician / cardiologist and the patient.

Treatment	Semi-urgent CABG	Elective CABG	
ASA	ASA should be continued in all patients with ACS who require CABG		
Ticagrelor	Suggested to discontinue a minimum of 48-72 hours prior to surgery to minimize the risk of bleeding.	Recommended to be discontinued ideally 5 days prior to surgery.	
Clopidogrel	Suggested to discontinue a minimum of 48-72 hours prior to surgery to minimize the risk of bleeding.	Recommended to be discontinued ideally 5 days prior to surgery.	
Prasugrel	Suggested to discontinue a minimum of 5 days prior to surgery to minimize the risk of bleeding.	Recommended to be discontinued ideally 7 days prior to surgery.	

Table 1: Risk of Perioperative Bleeding

LOW/VERY LOW RISK	MODERATE RISK	HIGH RISK
 Dental extractions (1 or 2 teeth), endodontic (root canal) procedure, Subgingival scaling or other cleaning Cataract surgery Dermatologic procedures (e.g. biopsy) Gastroscopy or colonoscopy without biopsies Coronary angiography Permanent pacemaker insertion or internal defibrillator placement (if bridging anticoagulation is not used) Gastroscopy or colonoscopy with biopsies Selected procedures (e.g. thoracentesis, paracentesis, arthrocentesis) 	 Other intra-abdominal surgery (e.g. laparoscopic cholecystectomy, hernia repair, colon resection) Other general surgery (e.g. breast) Other intrathoracic surgery Other orthopedic surgery Other vascular surgery Non-cataract ophthalmologic surgery Selected procedures (e.g. bone marrow biopsy, lymph node biopsy) Complex dental procedure (e.g. multiple tooth extractions) 	 Any surgery or procedure with neuraxial (spinal or epidural) anesthesia Neurosurgery (intracranial or spinal) Cardiac surgery (e.g. CABG, heart valve replacement) Major intra-abdominal surgery (e.g. intestinal anastomosis) Major vascular surgery (e.g. aortic aneurysm repair, aortofemoral bypass) Major orthopedic surgery (e.g. hip or knee replacement) Lung resection surgery Urological surgery (e.g. prostatectomy, bladder tumour resection) Extensive cancer surgery (e.g. pancreas, liver) Reconstructive plastic surgery Selected procedures (e.g. kidney biopsy, prostate biopsy, cervical cone biopsy, pericardiocentesis, colonic polypectomy)

OTHER RELEVANT THROMBOSIS CANADA CLINICAL GUIDES

- Acetylsalicylic Acid (ASA[®])
- Clopidogrel (Plavix[®])
- Prasugrel (Effient[®])
- Ticagrelor (Brilinta[®])

REFERENCES

Devereaux PJ, et al. Aspirin in patients undergoing noncardiac surgery. New Engl J Med 2014; 370: 1494-1503.

Graham M et al. Aspirin in patients with previous percutaneous coronary intervention undergoing noncardiac surgery. Ann Intern Med 2018;168(4):237-244.

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