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Perioperative Management of Antithrombotic Therapy: An American College of Chest Physicians Clinical Practice Guideline Executive Summary

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Abstract

Background: The American College of Chest Physicians Clinical Practice Guideline on the Perioperative Management of Antithrombotic Therapy addresses 43 patients-interventions-comparators-outcomes (PICO) questions related to the perioperative management of patients who are receiving long-term oral anticoagulant or antiplatelet therapy and require an elective surgery/procedure. This guideline is separated into 4 broad categories, encompassing the management of patients who are receiving: (i) a vitamin K antagonist (VKA), mainly warfarin; (ii) if receiving a VKA, the use of perioperative heparin bridging, typically with a low-molecular-weight heparin (LMWH); (iii) a direct oral anticoagulant (DOAC); and (iv) an antiplatelet drug.

Methods: Strong or conditional practice recommendations are generated based on high, moderate, low, and very low certainty of evidence using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) methodology for clinical practice guidelines.

Results: A multidisciplinary panel generated 43 guideline recommendations for the perioperative management of VKAs, heparin bridging, DOACs, and antiplatelet drugs of which 2 are strong recommendations: (i) against the use of heparin bridging in patients with atrial fibrillation; and (ii) continuation of VKA therapy in patients having a pacemaker or internal cardiac defibrillator (ICD) implantation. There are separate recommendations on the perioperative management of patients who are undergoing minor procedures, comprising dental, dermatological, ophthalmological, pacemaker/ICD implantation, and gastrointestinal (endoscopic) procedures.

Conclusions: Substantial new evidence has emerged since the 2012 iteration of these guidelines, especially to inform best practices for the perioperative management of patients who are receiving a VKA and may require heparin bridging, for the perioperative management of patients who are receiving a DOAC, and for patients who are receiving one or more antiplatelet drugs. Despite this new knowledge, uncertainty remains as to best practices for the majority of perioperative management questions.

Introduction

The perioperative management of antithrombotic therapy encompasses patients who are receiving a vitamin K antagonist (VKA), a direct oral anticoagulant (DOAC) or an antiplatelet drug and require a surgery or invasive procedure. An estimated 10-12 million people are assessed worldwide annually for perioperative anticoagulant management[1-3]. Since 2008, the American College of Chest Physicians (CHEST) Antithrombotic Guidelines has dedicated chapters addressing the perioperative management of patients who are receiving antithrombotic therapy[4,5]. The last iteration in 2012 addressed 11 Patients-Interventions-Comparators-Outcomes (PICO) questions that were separated into three domains, comprising perioperative management of vitamin K antagonists (VKAs), antiplatelet drugs, and heparin bridging[5].

The current CHEST Guidelines on Perioperative Antithrombotic Therapy on Perioperative Antithrombotic Therapy has expanded to address 43 PICO questions, with 44 associated recommendations. Overall, 39 of 43 recommendations achieved consensus in the first voting round, with the remainder achieving consensus in the second voting round. New domains that are addressed include the perioperative management of patients who are receiving a DOAC and those who receiving a $P2Y_{12}$ inhibitor antiplatelet agent, as well as guidance on perioperative laboratory testing. Since the last iteration, new clinical trial data has emerged that inform the perioperative management of heparin bridging in patients who are receiving a VKA, the perioperative management of patients who are taking DOACs, and the perioperative management of patients taking antiplatelet drugs. The guideline statements are intended primarily for clinicians who manage patients on antithrombotic therapy in perioperative settings but also may inform researchers in selecting questions for future studies, as well as patients and policy makers who are involved in patient care path development. This guideline is the first addressing the topic of the perioperative antithrombotic management that will be regularly updated as new evidence emerges according to the CHEST guideline policies[6].

The PICO questions and guideline statements are separated into 4 broad categories which reflect the patient groups assessed in clinical practice:

- Patients receiving a VKA, focused on warfarin.
- Among patients receiving a VKA, the use of perioperative heparin bridging.
- Patients receiving a DOAC.
- Patients receiving an antiplatelet drug.

The PICO questions are further arranged to reflect practical aspects of perioperative antithrombotic management, which includes:

- Interruption and resumption of VKAs before and after an elective surgery/procedure and need for perioperative heparin bridging.
- For patients in whom heparin bridging is considered, how to manage pre- and post-operative bridging during VKA interruption.
- Interruption and resumption of DOACs before and after an elective surgery/procedure.

- Perioperative management of antiplatelet therapy around non-cardiac surgery, cardiac surgery, mainly coronary artery bypass graft (CABG) surgery, and in patients with cardiac stents.
- Management of VKAs, DOACs and antiplatelet drugs around minor procedures, comprising dental, dermatological, ophthalmological, gastrointestinal endoscopy, and cardiac device implantation (pacemakers and internal cardiac defibrillators [ICDs]).

Qualifying remarks and definition of terms:

- This guideline addresses the perioperative antithrombotic management of patients who require an elective, non-urgent, surgery/procedure; it does not address patients who require an urgent surgery/procedure in whom the management paradigm differs considerably from that in the elective clinical setting[7].
- This guideline addresses the management of patients who are receiving long-term, typically ≥3 months, antithrombotic therapy and focuses on the most commonly used VKAs (warfarin), DOACs (apixaban, dabigatran, edoxaban, rivaroxaban), and antiplatelet drugs (aspirin [ASA], clopidogrel, prasugrel, ticagrelor); it does not address the management of drugs with anticoagulant or antiplatelet properties that are used infrequently (e.g., cilostozol, dipyridamole, pentoxyphylline) or that are used, typically, for short periods (e.g., NSAIDs).
- Perioperative antithrombotic management is anchored on the assessment of thromboembolic and bleeding risk based on patient- and surgery/procedure-related factors; this guideline provides risk classification schemes for thromboembolism and bleeding that are empiric but can aid patient management.
- The "perioperative period" or "perioperatively" is defined as the period focused before and after a surgery/procedure but, in its entirety, spans from one week before until 4 weeks after a surgery/procedure[8].
- "Heparin bridging" is defined as the pre- and/or post-operative administration of a therapeutic-dose regimen of low-molecular-weight heparin (LMWH) or unfractionated heparin (UFH), focusing on LMWH bridging, which is the most widely studied regimen and has the greatest potential for benefit (reduced thromboembolism) and potential trade-off of harm (increased bleeding)[4,5].

Notes on guideline methodology:
To facilitate understanding of the magnitude of any outcome, the symbols ↔, ↑, and ↓ accompany each Selected Summary of Findings to indicate whether the outcome Summary reports a point estimate per 1000 cases for the outcome and the confidence intervals. Certainty of evidence was based on the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) approach, and is categorized as high, moderate, low, or very low[9]. In the absence of high-quality evidence, it must be emphasized that providers will need to conduct an individualized assessment of patient- as well as procedural-related risk factors for bleeding and thrombosis in order to finalize any perioperative antithrombotic strategy based on these factors.

Perioperative antithrombotic management care pathways:

Based on the evidence presented, perioperative antithrombotic patient care pathways are shown in **Figure 1**, **Figure 2**, and **Figure 3**. These pathways can be used to inform individual patient management and to develop standardized care paths for clinics or institutions. **Figure 1** pertains to patients receiving a VKA and provides guidance on whether to interrupt VKA therapy perioperatively (if interruption is needed), how to interrupt VKA pre-operatively, whether to use heparin bridging therapy and how to bridge, and how to restart VKA and bridging therapy (if used) post-operatively. **Figure 2** pertains to patients receiving a DOAC and provides guidance on whether to interrupt DOAC therapy perioperatively, and if interruption is needed, how to interrupt DOAC therapy based on surgical/procedural bleed risk in the pre- and post-operative period. **Figure 3** pertains to patients who are receiving antiplatelet therapy and provides guidance on the timing of peri-operative interruption based on the type of antiplatelet agent (i.e., aspirin, clopidogrel, prasugrel, ticagrelor).

Section 1: Patients who are Receiving a VKA and Require an Elective Surgery or Procedure

Guideline Statement 1: ***In patients requiring VKA (warfarin) interruption for an elective surgery/procedure, we suggest stopping VKAs (warfarin) ≥5 days over an interruption of <5 days before an elective surgery/procedure. (Conditional recommendation, low certainty of evidence.)***

Guideline implementation considerations:

- *Providing a perioperative VKA management calendar that is distributed by paper or electronically to patients and clinicians has the potential to minimize VKA dosing errors and optimize communication.*
- *In selected patients, especially the elderly with comorbidities, patients with very low dose warfarin requirements, and those with a higher target INR range, a longer period of warfarin interruption may be needed.*
- *The interruption timing for non-warfarin VKAs will differ, as it is shorter for acenocoumarol (2-3 days) and longer for phenprocoumon (10-12 days).*

Guideline Statement 2: ***In patients requiring VKA (warfarin) interruption for an elective surgery/procedure, we suggest resuming VKA (warfarin) within 24 hours over a delay to >24 hours after an elective surgery/procedure. (Conditional recommendation, low certainty of evidence.)***

Guideline implementation considerations:

- *For most patients, resuming VKAs within 24 hours implies resumption on the evening of the surgery/procedure.*
- *Implicit in the early (within 24 hours) resumption of a VKA is that it takes, typically, 2-3 days for a partial anticoagulant effect and 5-6 days for a full anticoagulant effect to occur.*
- *VKA resumption may be delayed in certain postoperative circumstances, such as inadequate surgery/procedure-site hemostasis, an anticipated need for additional intervention, or patient inability to take oral medications.*

Guideline Statement 3: ***In patients requiring VKA (warfarin) interruption for an elective surgery/procedure, we suggest resuming the first post-operative VKA dose at the patient's usual dose over resuming VKA with double the usual dose. (Conditional recommendation, very low certainty of evidence.)***

Guideline implementation considerations:

- *Although postoperative doubling of the warfarin dose for 1-2 days may lead to a more rapid attainment of an INR ≥2.0 in some patients, there are concerns in applying this approach in practice, for example in patients with variable warfarin dose regimens and those expected to be hospitalized for >1 day.*

Guideline Statement 4: ***In patients requiring VKA interruption for an elective surgery/procedure who have an elevated INR (i.e., >1.5) 1-2 days before the surgery/procedure, we suggest against routine use of pre-operative vitamin K. (Conditional recommendation, very low certainty of evidence.)***

Guideline implementation considerations:

- *Uncertainty about routine preoperative vitamin K administration relates to the dose of vitamin K, limited availability of oral vitamin K formulations, and potential for resistance to postoperative re-anticoagulation.*

Guideline Statement 5: ***In patients receiving VKA therapy for a mechanical heart valve who require VKA interruption for an elective surgery/procedure, we suggest against heparin bridging. (Conditional recommendation, very low certainty of evidence.)***

Guideline implementation considerations:

- *In selected patients considered at high risk for thromboembolism, for example those with (i) an older-generation mechanical heart valve (i.e., tilting-disc valve), (ii) a mechanical mitral valve with one or more risk factors for thromboembolism, (iii) a recent (within last 3 months) thromboembolic event, or (iv) with prior perioperative thromboembolism, pre- and post-operative heparin bridging is suggested (see Guideline Statement 8).*

Guideline Statement 6: ***In patients receiving VKA therapy for atrial fibrillation who require VKA interruption for an elective surgery/procedure, we recommend against heparin bridging. (Strong recommendation, moderate certainty of evidence.)***

Guideline implementation considerations:

- *In selected patients considered at high risk for thromboembolism, for example those with a recent (< 3 month) history of stroke or transient ischemic attack or with a CHA_2DS_2VASc score ≥7 or $CHADS_2$ score of 5 or 6, pre- and post-operative heparin bridging is suggested (see Guideline Statement 8).*
- *A perioperative VKA and heparin bridging calendar (paper or electronic) that provides patients and clinicians an easy-to-use timetable for VKA interruption and resumption alongside the heparin bridging dosing regimen has the potential to minimize errors and optimize communication among caregivers.*

Guideline Statement 7: ***In patients receiving VKA therapy for VTE as the sole clinical indication who require VKA interruption for an elective surgery/procedure, we suggest***

against heparin bridging. (Conditional recommendation, very low certainty of evidence.)

Guideline implementation considerations:

- *Suggesting against bridging with a therapeutic-dose heparin regimen does not preclude the empiric use of a low-dose heparin regimen, typically started within 24 hours after surgery and continued for up to 5 days while VKA therapy is resumed, to decrease the risk for postoperative VTE.*
- *In selected patients considered at high-risk for VTE, for example those with a recent (< 3 months) history of VTE or other clinical situations associated with a high VTE risk (Table 1), pre- and post-operative heparin bridging is suggested (see Guideline Statement 8).*

Guideline Statement 8: ***In patients receiving VKA therapy who are classified as high-risk for thromboembolism and who require VKA interruption for an elective surgery/procedure, we suggest heparin bridging over no heparin bridging. (Conditional recommendation, very low certainty of evidence.)***

Guideline implementation considerations:

- *Stratification of patients according to perioperative thromboembolic risk, as shown in* ***Table 1****, is empiric as there are no clinical prediction models that have been validated in this clinical setting. The type of surgery may also affect thromboembolic risk, for example an anticipated higher risk in patients having open cardiac or major vascular surgery.*

Guideline Statement 9: ***In patients receiving VKA therapy who are classified as low-to-moderate risk for thromboembolism and who require VKA interruption for an elective surgery/procedure, we suggest against heparin bridging. (Conditional recommendation, very low certainty of evidence.)***

Guideline implementation considerations:

- *Although patients may be classified empirically as low-to-moderate risk for thromboembolism, there may be selected patients within this classification grouping (****Table 1****) in whom heparin bridging may be considered, for example patients with a prior history of perioperative thromboembolism.*

Management of VKAs around minor procedures (dental, dermatological, ophthalmological, pacemaker/ICD, colonoscopy with/without polypectomy)

Guideline Statement 10: ***In patients receiving VKA therapy who need a dental procedure, we suggest continuation of VKA over VKA interruption (Conditional recommendation, low certainty of evidence.)***

Guideline implementation considerations:

- *The risk for dental procedure-related bleeding may vary, being lower with single tooth extractions and higher with multiple tooth extractions or in patients with poor gingival health; accordingly, VKA interruption may be preferred in situations where oral bleeding is expected to be considerable.*

Guideline Statement 11: ***In patients receiving VKA therapy who need a dental procedure, we suggest using a pro-hemostatic agent with continuation of VKA over alternative management options (e.g., discontinuation of VKA with or without heparin bridging). (Conditional recommendation, low certainty of evidence.)***

Guideline implementation considerations:

- *Pro-hemostatic options include pre- and post-procedure administration of oral tranexamic acid mouthwash, 2-3 times daily, and intervention-specific measures (e.g., extra sutures, gauze soaked in tranexamic-acid).*

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Guideline Statement 12: ***In patients receiving VKA therapy who require a minor dermatologic procedure, we suggest continuation of VKA over VKA interruption. (Conditional recommendation, very low certainty of evidence.)***

Guideline implementation considerations:

- *The risk for dermatologic procedure-related bleeding may vary, being lower with resections of small (1-2 cm) skin cancers and biopsies, and higher with resections of larger (>3 cm) skin cancers, particularly if skin grafting is required; accordingly, VKA interruption may be preferred in situations where site-related bleeding is expected to be considerable or if lengthy wound healing is expected (e.g., skin graft).*

Guideline Statement 13: ***In patients receiving VKA therapy who require a minor ophthalmologic procedure, we suggest continuation of VKA over VKA interruption. (Conditional recommendation, very low certainty of evidence)***

Guideline implementation considerations:

- *VKA interruption may be preferred in patients considered at higher risk for bleeding, for example, those having more complex retinal surgery or patients having surgery with retrobulbar anesthesia. Cataract surgery is done usually with topical anesthesia and, less commonly, with retrobulbar anesthesia.*

Guideline Statement 14***: In patients receiving VKA therapy who require a pacemaker or ICD implantation, we recommend continuation of VKA over VKA interruption and heparin bridging. (Strong recommendation, moderate certainty of evidence.)***

Guideline implementation considerations:

- *Continuation of VKAs around cardiac device procedures is based on the premise that the patient's INR at the time of the procedure is <3.0.*

Guideline Statement 15***: In patients receiving VKA therapy who require VKA interruption for a colonoscopy with anticipated polypectomy, we suggest against heparin bridging during the period of VKA interruption. (Conditional recommendation, very low certainty of evidence.)***

Section 2: Perioperative Management of Patients who are Receiving Heparin Bridging

Guideline Statement 16: ***In patients receiving therapeutic-dose intravenous UFH bridging for an elective surgery/procedure, we suggest stopping UFH ≥4 hours before a surgery/procedure over stopping IV UFH <4 hours before a surgery/procedure. (Conditional recommendation, very low certainty of evidence.)***

Guideline Statement 17: ***In patients receiving therapeutic-dose intravenous UFH bridging for an elective surgery/procedure, we suggest resuming UFH ≥24 hours after a surgery/procedure over resuming UFH within 24 hours after a surgery/procedure. (Conditional recommendation, very low certainty of evidence.)***

Guideline implementation considerations:

- *When resuming UFH postoperatively, we suggest avoiding a bolus dose and commencing with a lower-intensity infusion that is associated with a lower target aPTT than that used for initiation of full-dose UFH administration.*

Guideline Statement 18: ***In patients receiving LMWH bridging for an elective surgery/procedure, we suggest administering the last pre-operative LMWH bridging dose at approximately 24 hours over administering the last dose 10-12 hours before a surgery/procedure. (Conditional recommendation, very low certainty of evidence.)***

Guideline Statement 19: ***In patients receiving LMWH bridging for an elective surgery/procedure, we suggest administering the first post-operative LMWH bridging dose at least 24 hours after a surgery/procedure over administering it less than 24 hours after a surgery/procedure. (Conditional recommendation, very low certainty of evidence.)***

Guideline implementation considerations:

- *We suggest waiting at least 24 hours before resuming LMWH bridging in patients having a low-to-moderate bleed risk surgery/procedure and waiting at least 48-72 hours before resuming LMWH bridging in patients having a high-bleed risk surgery/procedure (**Table 2**).*
- *For patients in whom the management plan is to delay resumption of LMWH bridging for 48-72 hours and who are considered at high risk for postoperative VTE, low-dose LMWH can be administered for the initial 2-3 days before the transition to LMWH bridging.*

Guideline Statement 20: ***In patients receiving LMWH bridging for an elective surgery/procedure, we suggest administering half the total daily dose of LMWH the day prior to the surgery/procedure over administering the full dose of LMWH the day prior. (Conditional recommendation, very low certainty of evidence.)***

Guideline implementation considerations:

- *This guidance may apply more to patients having a high-bleed-risk surgery, including patients having neuraxial (spinal or epidural) anesthesia, rather than in patients having a low-to-moderate bleed risk surgery/procedure (**Table 2**).*
- *Administering half the total daily dose of LMWH can be done by giving, on the morning of the day before the surgery/procedure, only the morning dose of a twice-daily LMWH regimen or ~50% of the dose of a once-daily LWMH regimen.*

Guideline Statement 21: ***In patients receiving LMWH bridging for an elective surgery/procedure, we suggest against routine measurement of anti-factor Xa levels to guide perioperative LMWH management. (Conditional recommendation, very low certainty of evidence.)***

Guideline implementation considerations:

- *There may be select patients undergoing high-bleed-risk surgeries/procedures (i.e., intracranial, spinal) or patients who require an urgent (non-elective) surgery/procedure where anti-factor Xa measurement may be considered.*

Section 3: Patients who are Receiving a DOAC and Require an Elective Surgery/Procedure

Guideline Statement 22: ***In patients receiving apixaban who require an elective surgery/procedure, we suggest stopping apixaban for 1-2 days, before the surgery/procedure over apixaban continuation. (Conditional recommendation, very low certainty of evidence.)***

Guideline implementation considerations:

- *The total duration of perioperative apixaban interruption will depend on the bleed risk associated with the surgery/procedure:*
  - *1 day off before low/moderate-bleed-risk;*
  - *2 days off before high-bleed-risk.*
- *This management may be applied irrespective of whether patients are receiving apixaban for atrial fibrillation or VTE.*

Guideline Statement 23: ***In patients receiving dabigatran who require an elective surgery/procedure, we suggest stopping dabigatran for 1-4 days before the surgery/procedure over dabigatran continuation. (Conditional recommendation, very low certainty of evidence.)***

Guideline implementation considerations:

- *The total duration of perioperative dabigatran interruption will depend on the bleed risk associated with the surgery/procedure and patient renal function:*
  - *1 day off before low/moderate-bleed-risk if CrCl ≥50 mL/min;*
  - *2 days off before low/moderate-bleed-risk if CrCl <50 mL/min;*
  - *2 days off before high-bleed risk if CrCl ≥50 mL/min;*
  - *4 days off for high-bleed-risk if CrCl <50 mL/min (this extended duration of interruption of >2 days reflects the unique management of patients who are receiving dabigatran and have a CrCl <50 mL/min)*
- *This management may be applied irrespective of whether patients are receiving dabigatran for atrial fibrillation or VTE.*

Guideline Statement 24: ***In patients receiving edoxaban who require an elective surgery/procedure, we suggest stopping edoxaban for 1-2 days before the surgery/procedure over edoxaban continuation. (Conditional recommendation, very low certainty of evidence)***

Guideline implementation considerations:

- *The total duration of perioperative edoxaban interruption will depend on the bleed risk associated with the surgery/procedure:*
    - *1 day off before low/moderate-bleed-risk;*
    - *2 days off before high-bleed-risk.*
- *This management may be applied irrespective of whether patients are receiving edoxaban for atrial fibrillation or VTE.*

Guideline Statement 25: ***In patients receiving rivaroxaban who require an elective surgery/procedure, we suggest stopping rivaroxaban for 1-2 days before the surgery/procedure over rivaroxaban continuation. (Conditional recommendation, very low certainty of evidence.)***

Guideline implementation considerations:

- *The total duration of perioperative rivaroxaban interruption will depend on the bleed risk associated with the surgery/procedure:*
    - *1 day off before low/moderate-bleed-risk;*
    - *2 days off before high-bleed-risk.*
- *This management may be applied irrespective of whether patients are receiving rivaroxaban for atrial fibrillation or VTE.*

Guideline Statement 26: ***In patients who require DOAC interruption for an elective surgery/procedure, we suggest against perioperative heparin bridging. (Conditional recommendation, very low certainty of evidence)***

Guideline implementation considerations:

- *The rapid offset and rapid onset of action of DOACs obviates the need for heparin bridging with short-acting anticoagulants such as UFH or LMWH in a perioperative setting.*

Guideline Statement 27: ***In patients who had DOAC interruption for an elective surgery/procedure, we suggest resuming DOACs >24 hours after a surgery/procedure over resuming DOACs within 24 hours. (Conditional recommendation, very low certainty of evidence.)***

Guideline implementation considerations:

- *The resumption of DOACs postoperatively will depend on the bleed risk associated with the surgery/procedure:*
    - *at least 24 hours after low/moderate-bleed-risk*
    - *48 - 72 hours after high-bleed-risk.*
- *DOACs have a rapid onset of action, with a peak effect occurring 1 - 3 hours after intake, thereby requiring cautious administration after a surgery/procedure.*

Guideline Statement 28: ***In patients who had DOAC interruption for an elective surgery/procedure, we suggest against routine DOAC coagulation function testing to guide perioperative DOAC management. (Conditional recommendation, very low certainty of evidence.)***

Guideline implementation considerations:

- *DOAC level testing may be considered, on a case-by-case basis, in non-elective perioperative clinical situations, for example, in patients who require an*

urgent/emergency surgery/procedure in whom DOAC level testing may inform the need for active DOAC reversal with administration of blood products or DOAC-specific reversal agents.

Section 4: Perioperative Management of Patients who are Receiving Antiplatelet Drugs

Guideline Statement 29a: ***In patients receiving ASA who are undergoing elective non-cardiac surgery, we suggest ASA continuation over ASA interruption. (Conditional recommendation, moderate certainty of evidence.)***

Guideline implementation considerations:

- *This guidance may be modified on a case-by-case basis. For example, in select patients undergoing a non-cardiac surgery associated with a high bleeding risk (e.g., intracranial, spinal); if ASA interruption is adopted, we suggest interruption for ≤7 days.*

Guideline Statement 29b: ***In patients receiving ASA therapy who are undergoing elective surgery and require ASA interruption, we suggest stopping ASA ≤7 days instead of 7-10 days before the surgery. (Conditional recommendation, very low certainty of evidence.)***

Guideline implementation considerations:

- *This suggestion may be modified on a case-by-case basis, depending on individual patient circumstances, for example, surgery-related bleeding risk.*

Guideline Statement 30: ***In patients receiving clopidogrel who are undergoing an elective non-cardiac surgery, we suggest stopping clopidogrel 5 days instead of 7-10 days before the surgery. (Conditional recommendation, very low certainty of evidence.)***

Guideline implementation considerations:

- *This suggestion may be modified on a case-by-case basis, depending on individual patient circumstances, for example, surgery-related bleeding risk.*

Guideline Statement 31: ***In patients receiving ticagrelor who are undergoing an elective non-cardiac surgery, we suggest stopping ticagrelor 3-5 days instead of 7-10 days before the surgery. (Conditional recommendation, very low certainty of evidence.)***

Guideline implementation considerations:

- *This suggestion may be modified on a case-by-case basis, depending on individual patient circumstances, for example, surgery-related bleeding risk.*

Guideline Statement 32: ***In patients receiving prasugrel who are undergoing an elective non-cardiac surgery, we suggest stopping prasugrel 7 days instead of 7-10 days before the surgery. (Conditional recommendation, very low certainty of evidence.)***

Guideline implementation considerations:

- *This suggestion may be modified on a case-by-case basis, depending on individual patient circumstances, for example, surgery-related bleeding risk.*

Guideline Statement 33: ***In patients who require antiplatelet drug interruption for an elective surgery/procedure, we suggest to resume antiplatelet drugs ≤24 hours instead of >24 hours after the surgery/procedure. (Conditional recommendation, very low certainty of evidence.)***

Guideline Statement 34: ***In patients who are receiving ASA and undergoing CABG surgery, we suggest continuation of ASA over interruption; in patients receiving a $P2Y_{12}$ inhibitor drug, we suggest interruption of the $P2Y_{12}$ inhibitor over continuation peri-operatively. (Conditional recommendation, low certainty of evidence)***

Guideline implementation considerations:

- *For pre-operative $P2Y_{12}$ interruption, we suggest:*
  - *7 days for prasugrel*
  - *5 days for clopidogrel*
  - *3-5 days for ticagrelor.*

Guideline Statement 35: ***In patients receiving ASA or a $P2Y_{12}$ inhibitor who are undergoing CABG surgery, we suggest resuming the ASA or the $P2Y_{12}$ inhibitor within 24 hours after surgery compared to ≥24 hours after surgery. (Conditional recommendation, low certainty of evidence.)***

Guideline implementation considerations:

- *Resumption of antiplatelet therapy may be delayed in patients who develop post-CABG thrombocytopenia (platelet count $<50{,}000\times10^9$/L), typically occurring with on-pump surgery.*

Guideline Statement 36: ***In patients receiving antiplatelet drug therapy who are undergoing an elective surgery/procedure, we suggest against the routine use of platelet function testing prior to the surgery/procedure to guide perioperative antiplatelet management. (Conditional recommendation, very low certainty of evidence.)***

Guideline implementation considerations:

- *Platelet function testing could be used with a possible small benefit and little harm in certain scenarios such as patients undergoing CABG surgery who have recently started taking a $P2Y_{12}$ inhibitor. Costs would be moderate for implementation.*

Guideline Statement 37: ***In patients receiving ASA and a $P2Y_{12}$ inhibitor with coronary stents placed within the last 6-12 weeks who are undergoing an elective surgery/procedure, we suggest either continuation of both antiplatelet agents or stopping one antiplatelet agent within 7-10 days of surgery. (Conditional recommendation, very low certainty of evidence.)***

Guideline implementation considerations:

- *Either approach is reasonable depending on the bleeding risk associated with the surgery/procedure if antiplatelet therapy is continued and risk for acute coronary syndrome/coronary stent thrombosis if antiplatelet therapy is interrupted.*
- *Several factors will weigh in the decision about whether to continue dual antiplatelet therapy or interrupt one agent including: the timing of stent*

placement (whether closer to 6 weeks or 12 weeks); the type of stent (drug-eluting or bare-metal); the location of the stent (whether at a dominant coronary artery or not); and the number and length of stents implanted.

Guideline Statement 38: ***In patients receiving ASA and a $P2Y_{12}$ inhibitor who had coronary stents placed within the last 3-12 months and are undergoing an elective surgery/procedure, we suggest stopping the $P2Y_{12}$ inhibitor prior to surgery over continuation of the $P2Y_{12}$ inhibitor. (Conditional recommendation, very low certainty of evidence.)***

Guideline implementation considerations:

- *This guidance is based on indirect evidence and expert-based consensus that stopping $P2Y_{12}$ inhibitors in patients with stents >3 months post implantation is likely safe.*
- *Several factors will weigh in the decision about whether to continue or interrupt the $P2Y_{12}$ inhibitor including: the timing of stent placement (whether closer to 3 months or 12 months); the type of stent (drug-eluting or bare-metal); the location of the stent (whether at a dominant coronary artery or not); and the number and length of stents implanted.*

Guideline Statement 39: ***In patients with coronary stents who require interruption of antiplatelet drugs for an elective surgery/procedure, we suggest against routine bridging therapy with a glycoprotein IIb-IIIa inhibitor, cangrelor, or LMWH over routine use of bridging therapy. (Conditional recommendation, low certainty of evidence.)***

Guideline implementation considerations:

- *A bridging approach may be considered in selected high-risk patients, for example in those with a recent (within 3 months) coronary stent in a critical location.*

Guideline Statement 40: ***In patient with coronary stents who require continued dual antiplatelet therapy, we suggest delaying an elective surgery/procedure over not delaying the surgery/procedure. (Conditional recommendation, very low certainty of evidence.)***

Guideline implementation considerations:

- *The duration of surgery/procedure delay is addressed on a case-by-case basis and should consider the urgency of the surgery/procedure, the time elapsed since coronary stenting and the risk profile of the coronary stenting (e.g., critical location, multiple stents).*
- *With regard to timing of cessation of $P2Y_{12}$ inhibitors or ASA we refer to the Guideline Statements 29a/b through 33.*

Management of antiplatelet drugs around minor procedures (dental, dermatological, ophthalmological)

Guideline Statement 41: ***In patients receiving an antiplatelet drug (ASA or $P2Y_{12}$ inhibitor) who are undergoing a minor dental procedure, we suggest continuing the antiplatelet drug (ASA or $P2Y_{12}$ inhibitor) over stopping the antiplatelet agent before the procedure. (Conditional recommendation, very low certainty of evidence.)***
Guideline implementation considerations:

- *Patients who are receiving dual antiplatelet therapy with ASA and a $P2Y_{12}$ inhibitor can continue ASA and interrupt the $P2Y_{12}$ inhibitor.*

Guideline Statement 42: ***In patients receiving an antiplatelet drug (ASA or $P2Y_{12}$ inhibitor) who are undergoing a minor dermatologic procedure, we suggest continuing the antiplatelet drug (ASA or $P2Y_{12}$ inhibitor) over stopping the antiplatelet agent before the procedure. (Conditional recommendation, very low certainty of evidence.)***
Guideline implementation considerations:

- *Patients who are receiving dual antiplatelet therapy with ASA and a $P2Y_{12}$ inhibitor can continue ASA and interrupt the $P2Y_{12}$ inhibitor.*

Guideline Statement 43: ***In patients receiving an antiplatelet drug (ASA or $P2Y_{12}$ inhibitor) undergoing a minor ophthalmologic procedure, we suggest continuing the antiplatelet drug (ASA or $P2Y_{12}$ inhibitor) throughout the ophthalmologic procedure over stopping the antiplatelet agent before the procedure. (Conditional recommendation, low certainty of evidence.)***
Guideline implementation considerations:

- *Patients who are receiving dual antiplatelet therapy with ASA and a $P2Y_{12}$ inhibitor can continue ASA and interrupt the $P2Y_{12}$ inhibitor.*

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Table 1. Adapted American College of Chest Physicians (CHEST) Suggested Risk Stratification for Patient-Specific Periprocedural Thromboembolism [4,5,8]

Risk Category	Mechanical Heart Valve	Atrial Fibrillation	Venous Thromboembolism
High (>10%/year risk of ATE or >10%/month risk of VTE)	Any mechanical mitral valve Caged ball or tilting disc valve in mitral/aortic position Recent (<3 month) stroke or TIA	CHA_2DS_2VASc score of ≥7 $CHADS_2$ score of 5 or 6 Recent (<3 month) stroke or TIA Rheumatic valvular heart disease	Recent (<3 month and especially 1 month) VTE Severe thrombophilia (deficiency of protein C, protein S or antithrombin; homozygous factor V Leiden or prothrombin gene mutation or double heterozygous for each mutation, multiple thrombophilias) Antiphospholipid antibodies Associated with vena caval filter Active cancer associated with high VTE risk**
Moderate (4%–10%/year risk of ATE or 4%–10%/month risk of VTE)	Bileaflet AVR *with* major risk factors for stroke*	CHA_2DS_2VASc score of 5 or 6 $CHADS_2$ score of 3 or 4	VTE within past 3-12 months Recurrent VTE Non-severe thrombophilia (heterozygous factor V Leiden or prothrombin gene mutation) Active cancer or recent history of cancer***
Low (<4%/year risk of ATE or <2%/month risk of VTE)	Bileaflet AVR *without* major risk factors for stroke*	CHA_2DS_2VASc score of 1-4 $CHADS_2$ score of 0–2 (and no prior stroke or TIA)	VTE more than 12 months ago

Legend:

*Atrial fibrillation, prior stroke or transient ischemic attack, hypertension, diabetes, congestive heart failure, age >75 years.

**Includes pancreatic cancer, myeloproliferative disorders, primary brain cancer, gastric cancer, esophageal cancer.

***Within 5 years if history of cancer, excluding non-melanoma skin cancer

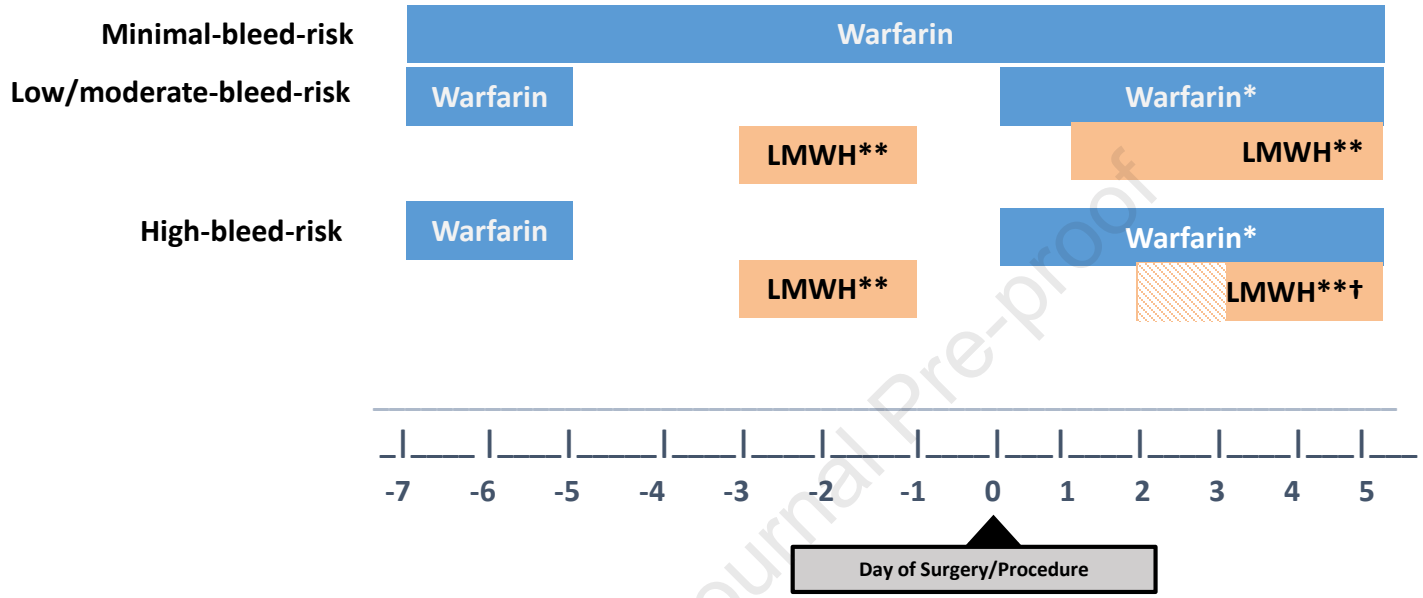
Table 2: Suggested Risk Stratification for Procedural Bleed Risk based on ISTH Guidance Statements[8]

High-Bleed-Risk Surgery/Procedure* (30-day risk of major bleed ≥ 2%)	– Major surgery with extensive tissue injury – Cancer surgery, especially solid tumor resection (lung, esophagus, gastric, colon, hepatobiliary, pancreatic) – Major orthopaedic surgery, including shoulder replacement surgery – Reconstructive plastic surgery – Major thoracic surgery – Urologic or Gastrointestinal surgery, especially anastomosis surgery – Transurethral prostate resection, bladder resection or tumor ablation – Nephrectomy, kidney biopsy – Colonic polyp resection – Bowel resection – Percutaneous endoscopic gastrotomy (PEG) placement, endoscopic retrograde cholangiopancreatography (ERCP) – Surgery in highly vascular organs (kidneys, liver, spleen) – Cardiac, intracranial, or spinal surgery – Any major operation (procedure duration >45 minutes) – Neuraxial anaesthesia† – Epidural injections
Low/Moderate-Bleed-Risk Surgery/Procedure (30-day risk of major bleed 0-2%)**	– Arthroscopy – Cutaneous/lymph node biopsies – Foot/hand surgery – Coronary angiography†† – Gastrointestinal endoscopy ±biopsy – Colonoscopy ±biopsy – Abdominal hysterectomy – Laparoscopic cholecystectomy – Abdominal hernia repair – Hemorrhoidal surgery – Bronchoscopy ±biopsy
Minimal-Bleed-Risk Surgery/Procedure* (30-day risk of major bleed ~0%)**	– Minor dermatologic procedures (excision of basal and squamous cell skin cancers, actinic keratoses, and premalignant or cancerous skin nevi) – Ophthalmological (cataract) procedures – Minor dental procedures (dental extractions, restorations, prosthetics, endodontics), dental cleanings, fillings – Pacemaker or cardioverter-defibrillator device implantation

Legend:
*No residual anticoagulant effect at time of procedure (i.e., 4-5 drug half-life interruption pre-procedure).

**Some residual anticoagulant effect allowed (i.e., 2-3 drug half-life interruption pre-procedure).
***Procedure can be safely done under full dose anticoagulation (may consider holding DOAC dose day of procedure to avoid peak anticoagulant effects).
†Includes spinal and epidural anesthesia or any other neuraxial (e.g., pain management) intervention; consider not only absolute risk for major bleeding but potentially devastating consequences of epidural bleeding and associated lower limb paralysis.
††Radial approach may be considered minimal bleed risk compared to femoral approach.

Figure 1. Perioperative Management of Vitamin K Antagonists (Warfarin)



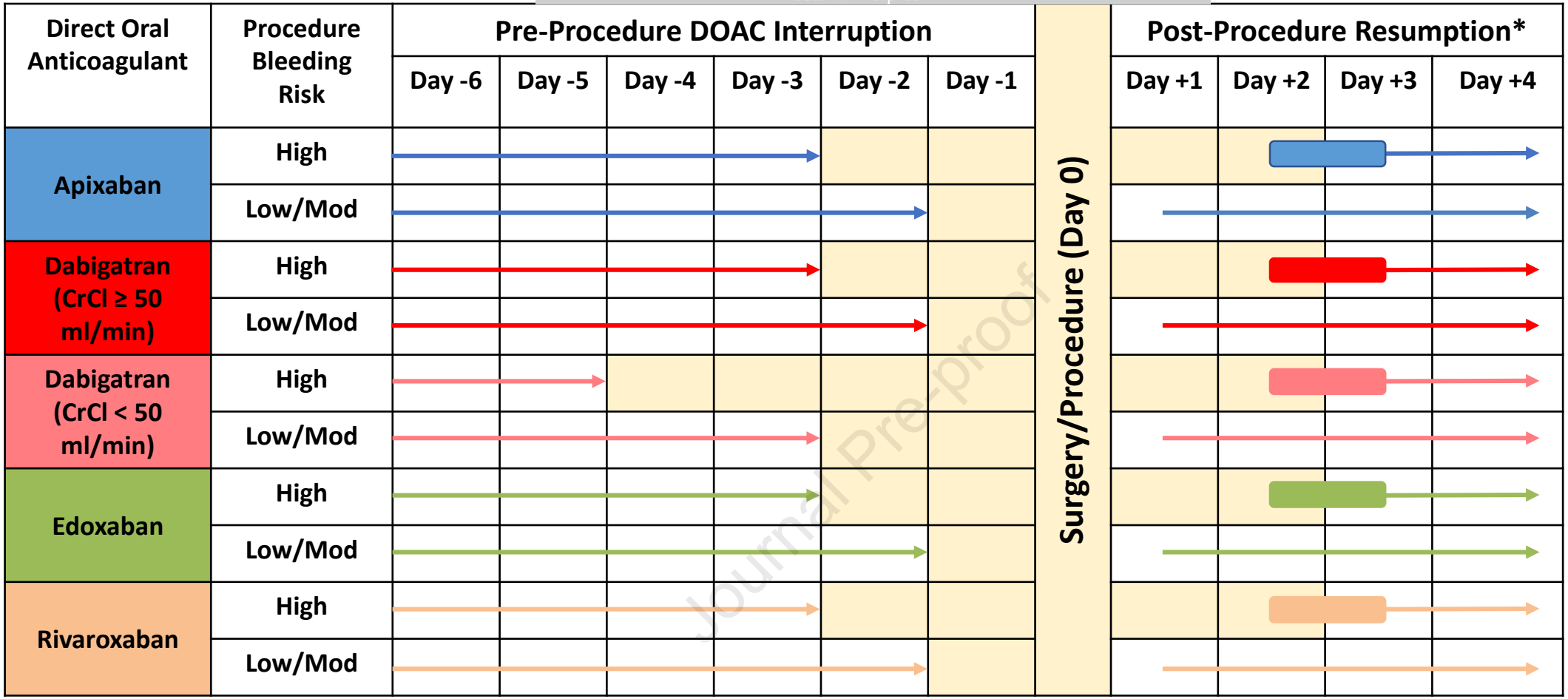
Legend

***Warfarin can be resumed on the evening of procedure (D0) for most patients, or the day after procedure (i.e., D1) at the patient's usual maintenance dose.

**Bridging suggested for high thrombotic risk populations with full-dose, subcutaneous LMWH (e.g., enoxaparin, 1 mg/kg bid or 1.5 mg/kg daily or dalteparin, 100 IU/kg bid or 200 IU/kg daily), with the last dose given the AM of the day prior to the procedure (i.e., D-1) at half the total daily dose.

†Low-dose LMWH (e.g., enoxaparin, 40 mg daily or dalteparin 5000 IU daily) can be used for VTE prophylaxis for first 24-72 hours post-procedure, with full dose LMWH resumed 2-3 days post-procedure.

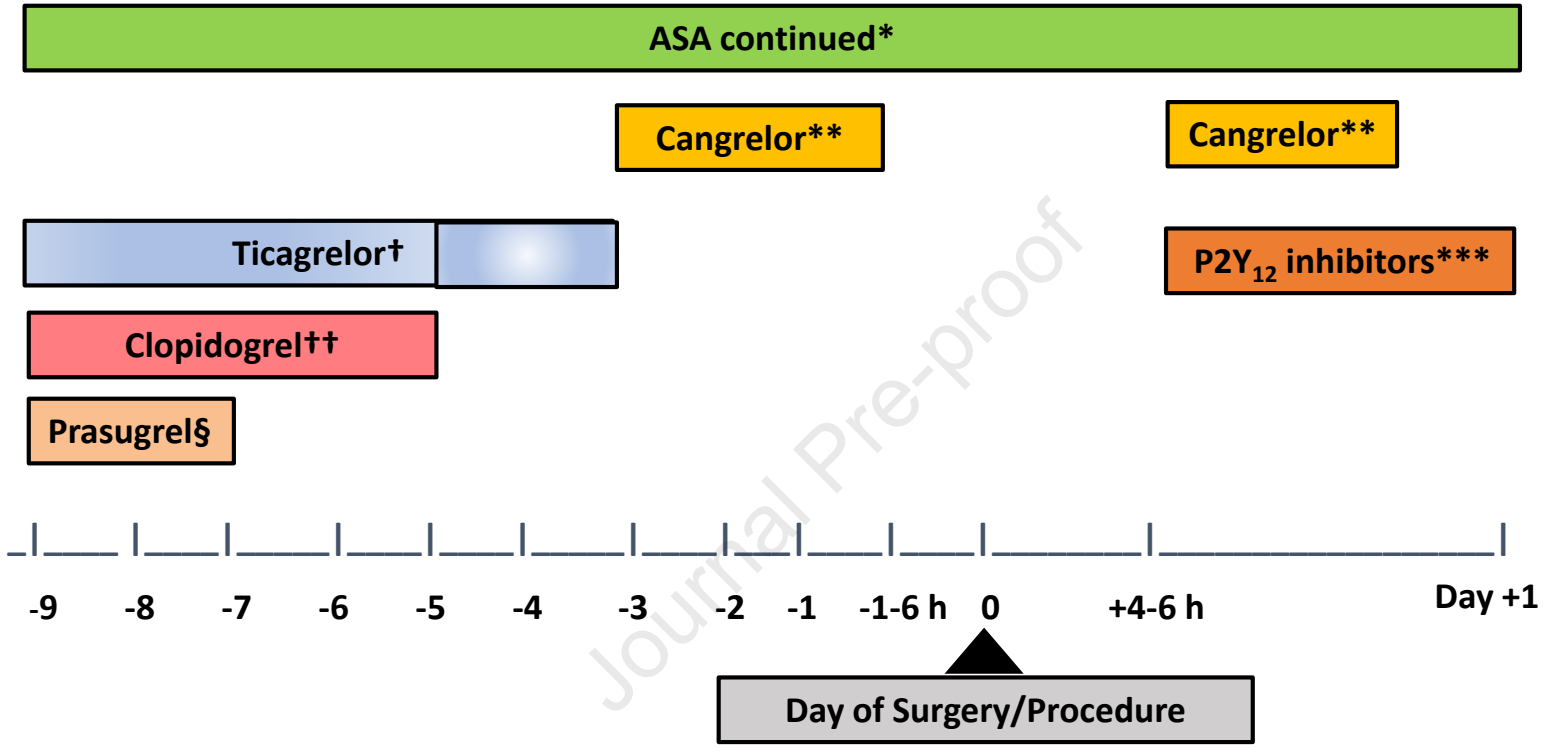
Figure 2. Perioperative Management of Direct Oral Anticoagulants



No DOAC administered that day

*DOAC can be resumed ~24 hours after low/moderate-bleed-risk procedures, and 48-72 hours after high-bleed-risk procedures. In selected patients at high risk for VTE, low-dose anticoagulants (i.e., enoxaparin, 40 mg daily or dalteparin, 5000 IU daily) can be given for the first 48-72 hours post-procedure.

Figure 3. Perioperative Management of Antiplatelet Drugs



Legend:

*Based on surgery/procedure bleed risk assessment.

**Routine use not suggested. If used, initiate within 72 hours from $P2Y_{12}$ inhibitor discontinuation at dose of 0.75 mg/kg/min; resume within 6 hours post-procedure for minimum of 48 hours and maximum of 7 days total. Very low quality data for antiplatelet bridging with glycoprotein IIb/IIIa inhibitors (e.g., eptifibatide, tirofiban).

***$P2Y_{12}$ inhibitors can be resumed within 24 hours post-procedure at a maintenance dose.

†For ticagrelor, 3-5 day interruption

††For clopidogrel, 5 day interruption

§For prasugrel, 7-10 day interruption.