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American College of Surgeons' Guidelines for the Perioperative Management of Antithrombotic Medication

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The aging of the population, along with advances in the treatment of chronic medical conditions, has increased the medical complexity of the average surgical patient. Currently, approximately 1 in 10 surgical patients is prescribed chronic anticoagulation.[1] In addition, dual agent antiplatelet therapy is commonly used for the secondary prevention of myocardial infarction and stent thrombosis after percutaneous coronary intervention. Perioperative management of these comorbidities is challenging because interruption transiently increases the risk of thromboembolism, while continuation of therapy increases the risk of surgical bleeding. Balancing the clinical consequences of these risks in the perioperative period is of utmost importance, as both adversely affect morbidity and mortality.[2,3]

In recent years, an influx of novel antithrombotic agents has made it difficult for surgeons to keep current with management guidelines. Despite this, surgeons are ultimately responsible for ensuring that their patients' antithrombotic medications are managed appropriately in the perioperative phase. Direct oral anticoagulants (DOACs) are a relatively new class of anticoagulants that are US Food and Drug Administration (FDA)-approved for the treatment of deep venous thrombosis (DVT) and pulmonary embolism (PE) and the prevention of thromboembolism in patients with nonvalvular atrial fibrillation. The DOACs have more predictable pharmacologic properties compared with the alternative (warfarin), with a rapid onset, short half-life, and no required routine lab monitoring. As such, there are an increasing number of patients who are prescribed DOACs who develop a surgical condition. Both prescribing physicians and patients are attracted to the predictable pharmacology that makes routine lab tests unnecessary. However, perioperative management has proven difficult given that only 1 medication (dabigatran) has an FDA-approved reversal agent (idarucizumab), and no widely available blood test exists that is suitable to monitor their effects on an individual's coagulation before embarking on an operation.

Guidelines for perioperative management of antithrombotic medications have been previously published by other professional organizations.[4-7] This document is intended to update, summarize, and combine this information into a clinically rigorous format suitable for a broad surgical readership. The objective of these guidelines is to update the surgeon reader in the following content areas: assess thromboembolic risk if the antithrombotic agent is discontinued perioperatively (Section I); determine the bleeding risk of the surgical procedure and patient factors that modify this risk (Section II); discuss heparin bridging for perioperative thromboembolism prevention in high risk patients (Section III); develop an evidence-based perioperative antithrombotic medication management strategy for elective surgical patients (Section IV); and outline perioperative antithrombotic medication management in the nonelective surgical setting (Section V).

METHODS

Previously published guidelines representing the official position of scientific societies form the basis of this perioperative antithrombotic medication management update.[4-7] Within the framework of existing guidelines,

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Abbreviations and Acronyms

DOACs = direct oral anticoagulants
INR = international normalized ratio
LMWH = low molecular weight heparin
PAD = peripheral artery disease
PCC = prothrombin complex concentrate
RR = relative risk
UFH = unfractionated heparin
VTE = venous thromboembolism

specific topics were identified through an iterative process that involved the review of existing guidelines and contemporary literature, as well as multi-iterative feedback from an internal expert panel. The topics were determined to be: thromboembolic risk assessment; perioperative bleeding risk assessment; perioperative heparin bridging guidelines and protocols; perioperative antithrombotic management strategies; and perioperative antithrombotic medication management in the nonelective setting. These topics were searched in PubMed for relevant articles published in the English language before March 1, 2018. Literature was sought out addressing knowledge gaps in previously published guidelines, namely, new antithrombotic medications (particularly direct oral anticoagulants [DOACs]), updated evidence around the indications for and utility of perioperative heparin bridging, and agent-specific "need-to-know" parameters relevant to surgical practice. We used the hierarchy of evidence and preferentially included systematic reviews with or without a meta-analysis, randomized controlled trials, observational design if the study was not covered in the systemic reviews and meta-analyses, and clinical guidelines from professional societies, where applicable. General exclusion criteria included editorials, case reports, and articles reporting interventions or outcomes that were not applicable to US hospitals. Therefore, all recommendations contained within these guidelines are based on level 1 or 2 evidence unless otherwise specified. The references were then reviewed by 2 team members working independently.

Guidelines were drafted by a primary author (MH) and a secondary author (AE) according to the evidence provided by the foundational guidelines and pertinent literature updates. The guidelines were then sent to an internal expert panel (CL, TD, DP, EJ, PC, PB), who served as members of the 2017-2018 American College of Surgeons' Board of Governors Practice Guidelines Workgroup, and external content experts for review and to reach consensus agreement on the final guidelines presented here. Case vignettes were developed by the authors based on the evidence presented in the guidelines and are contained within eDocument 1.

RESULTS

The antithrombotic medications commonly prescribed for long-term patient use are covered in Table 1. Table 2 summarizes all consensus statements and guidelines. The guidelines cover the assessment of perioperative thromboembolic risk secondary to the medical condition, the stratification of bleeding risk inherent to the procedure and the patient characteristics that modify this risk, the indications for heparin bridging and a recommended heparin bridging protocol, perioperative antithrombotic medication management recommendations, and considerations in the nonelective setting.

Section I: Estimating thromboembolic risk if antithrombotic agents are discontinued

The first step to developing a perioperative antithrombotic management strategy is to estimate the risk of a thromboembolic event occurring if the antithrombotic agent is discontinued perioperatively. Generally speaking, the clinical harm that results from a major perioperative bleeding event is likely less than for thrombosis. As an example, the case fatality rate for mechanical heart valve thrombosis is 17.5%,[14] venous thromboembolism (deep venous thrombosis or pulmonary embolism) is fatal in 5% to 10%,[15] embolic stroke is fatal in 37%,[16] and mortality from major bleeding on antithrombotic agents is estimated to be between 6% to 10%.[17]

Perioperative thromboembolic risk depends on several patient factors, most important of which is the medical indication for the antithrombotic agent. The medical indications covered in this section are nonvalvular atrial fibrillation, the presence of a mechanical heart valve, history of venous thromboembolism (VTE), inherited thrombophilias, peripheral arterial disease, and cerebrovascular disease. The thromboembolic risk stratification algorithm suggested here outlines risk according to the medical conditions covered in these guidelines, and is adapted from the 9th Edition American College of Chest Physicians' (CHEST) guidelines on the perioperative management of antithrombotic therapy (Table 3).[4] Here, thromboembolic risk is stratified into 3 risk groups (high, >10% annual risk for thromboembolism; moderate, 5% to 10% annual risk; and low, <5% annual risk) within each medical indication for chronic anticoagulation, based on indirect evidence from studies in the perioperative setting that determined the likelihood of developing a VTE for patients receiving less-effective (ie aspirin) or no anticoagulation.

Table 1. Antithrombotic Agents Commonly Encountered in the Surgical Setting

Agent	Medical indication	Mechanism of action	Half-life, h	Strategy for reversal	Last dose before operation
Unfractionated heparin	Arterial embolism or VTE prevention and treatment; treatment of atrial fibrillation with embolization; bridging therapy	Antithrombin III mediated selective inhibition of Factor Xa	1–2	Protamine sulfate	Intravenous: 2–6 h; subcutaneous: 12–24 h
Low-molecular-weight heparins; Enoxaparin (Lovenox, Sanofi-Aventis US LLC)	DVT treatment and prevention	Antithrombin III mediated selective inhibition of Factor Xa	2	Protamine sulfate (only partially effective)	24 h*
Warfarin (Bristol-Myers Squibb Co)	Stroke prevention in atrial fibrillation or cardiac valve replacement; DVT/PE treatment and prevention; recurrent MI prevention	Vitamin K antagonist	20–60	Vitamin K; 4-factor PCC[8]; FFP	5 d
Dabigatran etexilate (Pradaxa, Boehringer Ingelheim Pharmaceuticals, Inc)	Stroke prevention in atrial fibrillation; DVT/PE treatment and prevention	Direct thrombin inhibitor	8–15	Idarucizumab[9]; hemodialysis; 4-factor PCC[10]	24–48 h*
Rivaroxaban (Xarelto, Janssen Pharmaceuticals, Inc)	Stroke prevention in atrial fibrillation; DVT/PE treatment; DVT/PE prevention	Direct factor Xa inhibitor	5–13	4-factor PCC[11]	24–48 h*
Apixaban (Eliquis, Bristol-Myers Squibb Co)	Stroke prevention in atrial fibrillation	Direct factor Xa inhibitor	12	4-factor PCC[12]	24–48 h*
Edoxaban (Savaysa, Daiichi Sankyo, Inc)	Stroke prevention in atrial fibrillation; DVT/PE treatment and prevention	Direct factor Xa inhibitor	10–14	4-factor PCC[13]	24–48 h*
Aspirin	Prevention of MI, TIA, and CVA	Cyclooxygenase inhibitor	3–10	Platelet transfusion	7 d
Clopidogrel (Plavix, Bristol-Myers Squibb Co and Sanofi-Aventis US LLC)	Prevention and treatment of acute coronary syndrome; secondary prevention of coronary artery and stent thrombosis; treatment of peripheral arterial disease;	Irreversible ADP receptor antagonist	8	Platelet transfusion (only partially effective)	5–7 d

(Continued)

Table 1. Continued

Agent	Medical indication	Mechanism of action	Half-life, h	Strategy for reversal	Last dose before operation
	prevention of TIA and CVA				
Prasugrel (Effient, Daiichi Sankyo, Inc and Eli Lilly and Co)	Secondary prevention of coronary artery and stent thrombosis	Irreversible ADP receptor antagonist	7	Platelet transfusion (only partially effective)	5–7 d
Ticagrelor (Brilinta, AstraZeneca Pharmaceuticals, LP)	Secondary prevention of coronary artery and stent thrombosis; treatment of peripheral arterial disease; prevention of TIA and CVA	Reversible and noncompetitive ADP receptor antagonist	9	Platelet transfusion (more effective)	5–7 d

*Applies only to patients with normal renal function (CrCl> 50 mL/min).
ADP, adenosine diphosphate; CVA, cerebrovascular accident; DVT, deep venous thrombosis; FFP, fresh frozen plasma; MI, myocardial infarction; PCC, prothrombin complex concentrate; PE, pulmonary embolism; TIA, transient ischemic attack; VTE, venous thromboembolism.

Surgeons often stratify risk for patients undergoing surgery after a recent percutaneous coronary intervention. Dual agent antiplatelet therapy is commonly prescribed to prevent stent thrombosis after placement of a coronary stent. The recommended perioperative management of antiplatelet therapy after percutaneous coronary intervention is dependent on the type of cardiac stent used and the time elapsed since implantation, and although these decisions should always be made in close consultation with a cardiologist, evidence-based guidelines are described in detail later in this section.[18]

Nonvalvular atrial fibrillation

Nonvalvular atrial fibrillation is the most common medical indication for chronic anticoagulation. Thromboembolic risk for patients with nonvalvular atrial fibrillation is best determined through assessment of individual patient risk factors. The CHA_2DS_2-VASc score (Congestive heart failure [+1], Hypertension [+1], Age ≥75 years [+2], Diabetes [+1], previous Stroke/transient ischemic attack/thromboembolism [+2], Vascular disease, Age 65 to 74 years [+1], Sex category female [+1]) estimates the risk for thromboembolism in patients with atrial fibrillation by assigning points to risk factors as described previously.[19] Patients with a CHA_2DS_2-VASc score of 1 to 3 are considered low risk (<5% annual risk of VTE), those with a score of 4 to 5 are considered moderate risk (5% to 10% annual risk of VTE), and those with a score ≥ 6 are considered high risk (>10% annual risk of VTE).[19] Although the CHA_2DS_2-VASc score has not been prospectively validated in the perioperative setting, this tool has been used to estimate thromboembolic risk if anticoagulation is held, and to determine whether heparin bridging is indicated perioperatively (guidelines for heparin bridging are discussed further in Section III).

Prosthetic heart valves

Perioperative thromboembolic risk inherent to mechanical prosthetic heart valves is dependent on the type, number, and location of the valvular prosthetic, as well as the presence of additional cardiac risk factors (atrial fibrillation, previous stroke or transient ischemic attack [TIA], hypertension, diabetes, congestive heart failure, age > 75 years).[20] Patients with mechanical bileaflet aortic valve prostheses without previous stroke or atrial fibrillation fall into the low annual risk category (<5% annual rate of thromboembolism when anticoagulated with warfarin).[21] Moderate risk patients (5% to 10% annual stroke risk when on warfarin anticoagulation) comprised those with mechanical bileaflet aortic valve prostheses with atrial fibrillation. Finally, high-risk patients have a >10% annual risk of stroke while anticoagulated, and

Table 2. Summary of Guidelines for the Perioperative Management of Antithrombotic Medications

Clinical area	Guideline
Preoperative thromboembolic risk stratification	
Nonvalvular atrial fibrillation thromboembolic risk	Stratify thromboembolic risk using the CHA_2DS_2-VASc score
Prosthetic heart valve thromboembolic risk	Stratify risk according to valve type, location, and individual thromboembolic risk factors (atrial fibrillation, history of thromboembolism).
Venous thromboembolism thromboembolic risk	Stratify based on time elapsed since VTE diagnosis and individual risk factors (cancer, thrombophilia); elective operation should be deferred for ≥3 mo after VTE diagnosis.
Coronary artery disease coronary thromboembolism risk	Elective operation should be deferred for ≥14 d for balloon angioplasty, 30 d for bare-metal stent placement, and 1 year for drug-eluting stent placement.
Stroke thromboembolic risk	Elective operation should be deferred for ≥9 mo after an ischemic stroke.
Peripheral arterial disease thromboembolic risk	Patients presenting for surgical evaluation who receive antithrombotic medication for symptomatic peripheral arterial disease should be managed in close consultation with a vascular specialist or vascular surgeon.
Procedural bleeding risk stratification	
Bleeding risk inherent to patient characteristic	Stratify risk using the HAS-BLED score.
Bleeding risk inherent to the procedure	Largely a subjective decision on behalf of the operating surgeon; most operations under the purview of the general surgeon will be classified as at least "low risk."
Perioperative bridging therapy	
Antiplatelet therapy	Currently there is no evidence to suggest a benefit from the use of antiplatelet bridging therapy perioperatively.
Direct oral anticoagulant therapy	Currently there is no evidence to suggest a benefit from the use of heparin bridging in patients taking DOACs.
Warfarin therapy	Use for those classified as high VTE risk; discontinue warfarin 5 d before an elective procedure, and when the INR falls below the patient's therapeutic range, begin LMWH at a therapeutic dose until 24 h before the procedure; reinitiate warfarin 12 to 24 h after operation; reinitiate LMWH 48 to 72 h after operation.
Perioperative antithrombotic medication management strategy	
Unfractionated heparin	
Intravenous	Hold 4 to 6 h before elective operation.
Subcutaneous	Hold 12 to 24 h before elective operation.
Low-molecular-weight heparin	Hold 24 h before operation; resume 48 to 72 h after operation.
Warfarin	Hold for 5 d before an elective operation; resume at previous dosing levels 12 to 24 h after operation.
Dabigatran	
Normal renal function	Hold for 2 d before high bleeding risk operation and 1 day before low bleeding risk operation; resume 2 to 3 d after high-bleeding risk operation and 1 day after low bleeding risk operation.
Impaired renal function	Hold for 4 d before high bleeding risk operation and 2 d before low bleeding risk operation.
Rivaroxaban, apixaban, edoxaban	Hold for 2 d before high bleeding risk operation and 1 day before low bleeding risk operation; resume 2 to 3 d after high bleeding risk operation and 1 day after low bleeding risk operation.
Aspirin	Hold aspirin for 7 to 10 d before high bleeding risk operation in patients who have not had a percutaneous coronary intervention (PCI); resume when bleeding risk has diminished; in patients with recent PCI, consult with cardiologist.
Clopidogrel, prasugrel, ticagrelor	Hold 5 to 7 d before low and high bleeding risk operation; resume when bleeding risk has diminished.

(Continued)

Table 2. Continued

Clinical area	Guideline
Consideration in the nonelective setting	
Vitamin K antagonist	Administer vitamin K and 4-factor PCC to patients with an elevated INR secondary to warfarin who are actively bleeding and/or require urgent operation.
Dabigatran	Administer idarucizumab to patients with evidence of significant dabigatran levels (by history of ingestion or laboratory parameter) who are bleeding or require emergency operation.
Other DOAC	Administer 4-factor PCC transfusion (50 units/kg) for partial reversal in patients with evidence of active factor Xa inhibitor as needed in emergency situation.
Anti-platelet agent	Transfuse 1 pooled unit of platelets immediately before operation and redose as needed for ongoing bleeding.

DOAC, direct oral anticoagulant; LMWH, low-molecular-weight-heparin; PCC, prothrombin complex concentrate; PCI, percutaneous coronary intervention; VTE, venous thromboembolism.

include patients with any mitral-valve prosthesis, any caged-ball or tilting-disk aortic-valve prosthesis, multiple mechanical heart valves, or previous thromboembolic event.[20]

Patients with bioprosthetic (ie nonmechanical) heart valves, whether porcine or bovine in nature, do not require long-term anticoagulation for the valve alone.[20,22] All transcutaneous placed aortic valves are bioprosthetic in nature. Many guidelines and surgeons recommend short-term anticoagulation (ie 3 to 6 months) immediately after implantation of a bioprosthetic valve until the fabric of the sewing ring has become endothelialized, in order to decrease the incidence of thromboembolic events.[20,22] If one encounters a patient with a bioprosthetic valve on anticoagulation (that is more than 3 months out from the operation), they are being anticoagulated for a secondary reason. That reason should be included in a risk/benefit analysis about whether to stop anticoagulation. Elective operations should be delayed for 3 to 6 months after implantation of a bioprosthetic valve. However, in the event of a nonelective operation, the surgeon should have no hesitancy in stopping warfarin without any bridging methodology and restarting it only when there is no increased risk of bleeding.[20]

Venous thromboembolism

Recent thromboembolism (within 3 months) portends a high risk for recurrent thromboembolism in the perioperative phase if anticoagulation is discontinued. It is estimated that premature cessation of anticoagulation in the first month after an acute VTE is associated with a 40% 1-month risk of recurrent VTE, and 10% for the subsequent 2 months.[23,24] After completion of 3 months of anticoagulation treatment, the annual risk for recurrent VTE falls to 15%.[23,24] It follows that as a general rule, elective surgery should be deferred for at least 3 months after a diagnosis of VTE.[4]

The risk of VTE recurrence in the event that anticoagulation is held also depends on whether the VTE was provoked or unprovoked,[25] and the presence of underlying risk factors such as cancer or inherited thrombophilia.[25] Provoked VTEs are defined as VTEs with an identifiable

Table 3. Risk-Stratification for Perioperative Thromboembolism

Risk category	Mechanical heart valve	Atrial fibrillation	Venous thromboembolism
High	Mitral valve prosthesis; caged-ball or tilting disc aortic prosthesis; stroke or TIA within 6 mo	CHA_2DS_2-VASc score $\geq$ 6; stroke or TIA within previous 3 mo; rheumatic valvular heart disease	VTE within 3 mo; severe thrombophilia*
Moderate	Bi-leaflet aortic valve prosthesis and at least one of the following risk factors: atrial fibrillation, previous stroke or TIA, hypertension, diabetes, congestive heart failure, age > 75 y	CHA_2DS_2-VASc score 4 to 5 or previous stroke or TIA more than 3 mo before	VTE within 3 to 12 mo; nonsevere thrombophilia†; recurrent VTE; active cancer
Low	Bi-leaflet aortic valve prosthesis and no other risk factors for stroke	CHA_2DS_2-VASc score 2-3 (assuming no previous stroke or TIA)	VTE > 12 mo previous and no other risk factor

(Modified from Douketis and colleagues[4] with permission from the American College of Chest Physicians 9th Edition Perioperative Antithrombotic Management Guidelines).
*Severe thrombophilia is defined as deficiency in protein C, protein S, or antithrombin; antiphospholipid antibodies; and those with multiple abnormalities.
†Nonsevere thrombophilia is defined as heterozygous factor V Leiden or prothrombin gene mutation.
TIA, transient ischemic attack; VTE, venous thromboembolism.

factor, such as an inciting event (ie surgery, long flight, hospital admission), transient major risk factors (ie major surgery > 30 minutes hospitalization or immobility, pregnancy, estrogen therapy), or permanent risk factors (ie inherited thrombophilias, chronic heart failure, inflammatory bowel disease, malignancy).[26] Patients with recent (within the past 3 months) VTE, with severe thrombophilia (protein C, protein S, or antithrombin deficiency, antiphospholipid syndrome, homozygous for factor V Leiden, homozygous for prothrombin gene mutation),[27] or with active cancer are classified as high thrombotic risk (annual VTE risk > 10%). A VTE within the previous 3 to 12 months, nonsevere genetic thrombophilia (heterozygous for factor V Leiden, heterozygous for prothrombin gene mutation),[27] and recurrent thromboembolism patients are classified as moderate annual risk (5% to 10%). Finally, patients 1-year past VTE diagnosis are classified as low thromboembolic risk (<5% annually). Controversy exists as to the optimal duration of anticoagulation prescribed to patients diagnosed with an unprovoked VTE, and it follows that the perioperative anticoagulation management of these patients is also controversial. We suggest close consultation with the prescribing physician when developing a perioperative anticoagulation strategy for patients with a history of an unprovoked VTE or a provoked or unprovoked life-threatening pulmonary embolism.[25]

Inherited thrombophilia

Inherited thrombophilia is a genetic tendency to develop venous thromboembolic disease. These patients may be prescribed chronic anticoagulation for thromboembolism risk reduction and/or may require special consideration when administering prophylactic anticoagulation postoperatively. Factor V Leiden is the most common inherited thrombophilia, with an estimated prevalence of 4% to 5% within Caucasian populations, and it increases the relative risk (RR) of spontaneous VTE by 5-fold.[28] Deficiencies in protein S, protein C, and antithrombin account for the majority of the remaining cases.[29,30] Indefinite anticoagulation after an acute VTE is advised for patients with inherited thrombophilia with history of an unprovoked VTE, life-threatening pulmonary embolism, extensive proximal deep venous thrombosis, male sex, strong family history, or more than 1 inherited thrombophilia.[6] Patients who have a VTE history with severe thrombophilia (eg, deficiency in protein C, protein S, or antithrombin; antiphospholipid antibodies; and those with multiple abnormalities) should be classified as high-risk for perioperative thromboembolism. Patients who have a VTE history with nonsevere thrombophilia (eg, heterozygous factor V Leiden or prothrombin gene mutation) should be stratified as moderate perioperative thromboembolic risk.[31] Consultation with the prescribing physician when developing perioperative management plans in these patients is highly recommended.

Coronary artery disease

Daily low-dose aspirin therapy (75 to 100 mg) is recommended by the US Preventive Services Task Force and the American Heart Association for the primary and secondary prevention of atherosclerotic cardiovascular disease.[7,32,33] Dual antiplatelet therapy is prescribed after coronary stent placement to prevent stent thrombosis, the duration of which is dependent on stent type (ie bare metal vs drug eluting) as well as the indication for placement (ie stable angina vs myocardial infarction).[34] The risk of stent thrombosis is highest within 4 to 6 weeks of stent placement, and discontinuation of dual antiplatelet therapy is a strong risk factor for stent thrombosis.[35]

An estimated 5% of patients with coronary stents require noncardiac surgery within 1 year of coronary stent implantation; 23% within 5 years.[36] In these patients, risk of cardiac complications from the discontinuation of antiplatelet therapy needs to be weighed against major surgical bleeding risk. Dual agent antiplatelet therapy is currently recommended for at least 6 to 12 months after placement of bare-metal stents and drug-eluting stents.[37] Elective surgery should be deferred for at least >14 days after balloon angioplasty, 30 days after bare-metal stent placement, and 1 year after drug-eluting stent placement.[7] Elective surgery can be considered 180 days after drug-eluting stent placement if surgical delay outweighs the potential harms of stent thrombosis.[7] In situations in which surgery cannot be deferred, a discussion with the prescribing cardiologist concerning the risk/benefit ratio of stopping antiplatelet therapy should be pursued, and patient disclosure should be documented.[7]

Stroke

Low-dose aspirin therapy and/or clopidogrel is recommended for treatment of acute ischemic stroke and secondary prevention after ischemic stroke or TIA.[38] In a large observational study, recent history of ischemic stroke was significantly associated with major cardiovascular events after elective noncardiac surgery (for stroke within 3 months: odds ratio [OR] 14.23, 95% confidence interval [CI] 11.61 to 17.45). The elevated risk for cardiac events plateaued at 9 months after ischemic stroke.[39] Therefore, we recommend that elective surgery should be deferred, if possible, for at least 9 months after ischemic stroke.

Peripheral arterial disease

Dual antiplatelet therapy is recommended for patients with peripheral arterial disease (PAD) with ischemic limb symptoms and clinically significant coronary or cerebrovascular disease, and a single agent (aspirin, clopidogrel, or ticagrelor) is recommended for patients with PAD without clinically significant coronary or cardiovascular disease.[40] Chronic warfarin therapy has been shown to improve long-term graft patency in select patients with high-risk surgical bypass grafts, such as after vein bypass using a suboptimal conduit and/or compromised distal runoff, or after prosthetic graft bypass.[41,42] Although the risks and benefits of perioperative cessation in PAD are not well defined, patients on antithrombotic agents to promote long-term patency of high-risk surgical revascularization conduits should be considered at high thromboembolic risk perioperatively, and their antithrombotic medications should be managed accordingly. Patients presenting for surgical evaluation who receive antithrombotic medications for symptomatic peripheral arterial disease should be managed in close consultation with a vascular specialist or vascular surgeon.

Section II: Defining procedural bleeding risk

Each patient's individualized bleeding risk assessment should consider the invasiveness of the surgery, the consequences of bleeding if bleeding does occur, and the patient's medical history, particularly comorbidities that have an impact on hemostasis and/or coagulation.[43] A detailed history should elicit patient characteristics that increase bleeding risk, focusing on previous surgery, trauma, family history, and current antithrombotic medications.[44] The HAS-BLED score (**H**ypertension, **A**bnormal renal/liver function, **S**troke, **B**leeding history or predisposition, **L**abile INR, **E**lderly, **D**rugs/alcohol concomitantly) is a useful tool for predicting major bleeding in anticoagulated patients with nonvalvular atrial fibrillation according to the risk factors described within its acronym.[45] Each risk factor earns 1 point, and a score ≥ 3 indicates "high bleeding risk" (5.8% yearly risk). The HAS-BLED score has been demonstrated to be a valid and reliable predictor of bleeding events during perioperative heparin bridging of chronic oral anticoagulation.[46]

The bleeding risk inherent to the procedure or operation is determined based on the invasiveness of the procedure and the sequelae of bleeding if it occurs. Available evidence on periprocedural bleeding risk in patients on antithrombotic therapy is of low quality, and is based largely on case series data alone. Certain minimally invasive procedures like dental extraction, cataract removal, joint injections, and diagnostic endoscopic procedures have minimal bleeding risk and do not require discontinuation of antithrombotic agents.[47,48] Although some guidelines and reviews have grouped procedures into lower or higher bleeding risk,[49-51] we recommend that surgeon experience inform the decision around bleeding risk inherent to the procedure, and that decisions around the management of antithrombotic medications be made with each individual patient based on their goals of care. Postoperative physical exam focusing on assessment of the wound, hematomas, etc, will inform the safety of resumption of an antithrombotic agent postoperatively.

Due to the relative lack of evidence contributing to published bleeding risk stratification guidelines, the operating surgeon should focus his or her bleeding risk assessment on the risk of bleeding based on the patient's individual anatomy, pathology, risk factors, and their clinical experience with the surgical procedure at hand.

Section III: When to consider perioperative bridging

Heparin bridging is the substitution of long-acting anticoagulants with short-acting agents in preparation for an invasive procedure. The goal of bridging anticoagulation therapy is to minimize the high-risk patient's risk for VTE while also minimizing their risk of bleeding after a high-risk procedure. Heparin bridging therapy is used almost exclusively for high-VTE-risk patients on chronic warfarin therapy. The rapid onset of action and predictable half-lives of DOACs makes bridging therapy unnecessary in the perioperative period.[50] There is no evidence to support a benefit from antiplatelet bridging therapy for surgical procedures that require antiplatelet cessation.[4,52]

Periprocedural heparin bridging is a common practice, and heparin-based bridging protocols are well described.[53,54] When using heparin bridging therapy, it is important to closely monitor for heparin-induced thrombocytopenia, which will manifest as a drop in platelet count and paradoxical thrombosis. Recently, low-molecular weight heparin (LMWH) has largely taken the place of unfractionated heparin (UFH) as the primary agent used for bridging therapy, due to the ability to administer LMWH safely on an outpatient basis while maintaining a low incidence of bleeding complications.[55] A therapeutic dose of LMWH (1 mg/kg twice daily) is now the standard of practice.

High-quality data regarding the utility of periprocedural bridging remains limited, but in general, it is recommended only for patients who have high perioperative VTE risk if anticoagulation is discontinued.[56] The utility of heparin bridging for patients taking warfarin for thromboembolism prevention due to atrial fibrillation was analyzed in a randomized controlled trial for the first time in 2015. Douketis and colleagues[57] found that the

incidence of arterial thromboembolism was equivalent between patients on LMWH bridging therapy and patients on placebo, and that patients on LMWH bridging therapy had a significantly higher rate of major hemorrhage (3.2% vs 1.3%, $p < 0.005$). However, the study did have important limitations that warrant further investigation. The study did not differentiate between patients who were at low vs high risk for VTE. Most patients included in the study were low VTE risk, (the mean $CHADS_2$ score was 2.3) and only 3% of the patient population had a high $CHADS_2$ score (5 or 6). Consequently, these results may not apply to patients with higher thromboembolic risk. Patients who are high VTE risk ($CHADS_2$ scores of 5 to 6) have a 12% to 18% annual stroke rate, and may very well benefit from bridging therapy.[58] Therefore, the use of bridging therapy for patients with nonvalvular atrial fibrillation and at high perioperative risk for VTE (previous stroke/embolic event, cardiac thrombus, or $CHADS_2$ score $\geq$ 5 to 6 or CHA_2DS_2-VASc score of $\geq$ 6) should be considered.

The utility of heparin bridging in patients on warfarin for VTE prevention/treatment and for thromboembolism prevention secondary to mechanical heart valve has not been thoroughly investigated. Expert consensus has defined 2 patient populations that should be bridged perioperatively due to high risk of VTE:

1) Mechanical heart valve: patients with a mitral-valve replacement, $\geq$2 mechanical valves, non-bi-leaflet aortic-valve replacement, or aortic-valve replacement with previous stroke, TIA, intracardiac thrombus, or cardioembolic event.[49]

2) Patients with a VTE occurrence within the past 3 months, and patients who have had a VTE while on therapeutic anticoagulation.[49]

Our recommended approach to bridging therapy is consistent with the American College of Chest Physicians (ACCP) 9th Edition guidelines on perioperative management of antithrombotic therapy.[4] We recommend discontinuing warfarin 5 days before an elective procedure, and when the international normalized ratio (INR) falls below the patient's therapeutic range, begin LMWH at a therapeutic dose, and administer until 24 hours before the procedure. The INR is performed on the morning of the procedure. Intravenous vitamin K (single 1-mg dose) should be administered if above INR is above 1.5. For high risk bleeding operations, warfarin is reinitiated within 12 to 24 hours (the evening of or the following morning) at the previous dose, and therapeutic dose LMWH should be restarted 48 to 72 hours after surgery. Once the INR is in the therapeutic range (usually about 5 days later), heparin bridging therapy can be discontinued. In patients with renal insufficiency (creatinine clearance [CrCl] < 30 mL/min), unfractionated heparin is preferred over LMWH, which is renally eliminated.

Section IV: Building a perioperative management strategy for antithrombotic medications

Perioperative management strategies for elective surgery are formed by carefully balancing the risk for thromboembolism against the risk for major periprocedural bleeding. These decisions should be conducted in a patient-centered manner (ie discussion with patients and caregivers, if applicable) and made in close consultation with the initial prescribing physician to ensure evidence-based planning and continuity of care. Case vignettes that serve to guide surgeons through the decision-making process described here are available in eDocument 1.

If the (noncardiac) procedure requires interruption of the patient's antithrombotic therapy (defined as low or high bleeding risk), the half-life of the antithrombotic agent will largely determine the timing for discontinuation, and the onset of action will guide postoperative resumption. Table 4 contains a summary of preoperative management strategies, stratified by the patient's thromboembolic risk (Section I) and procedural bleeding risk (Section II).

Nonoral anticoagulants (when used for heparin bridging)

Rapid onset, nonoral anticoagulants used for heparin bridging include UFH and LMWH. In patients receiving UFH at a therapeutic dose (80 units/kg IV bolus followed by an initial continuous infusion of 18 units/kg/hour)[59] for the purposes of heparin bridging, the infusion should be stopped 4 to 6 hours before high bleeding risk procedures.[4,60] Therapeutic-dose LMWH (enoxaparin 1 mg/kg subcutaneously twice daily) used for bridging should be held for at least 24 hours before surgery.[4,61] If deemed safe by the operating surgeon, UFH/LMWH can be resumed 24 hours after low risk surgery and 48 to 72 hours after high risk bleeding surgery.[4] Premature resumption of heparin bridging anticoagulation should be avoided as it is associated with major bleeding rates 4 times that of baseline.[55]

Vitamin K antagonists

Patients prescribed warfarin for chronic anticoagulation, who require discontinuation for a surgical procedure, should hold warfarin for 5 days before the procedure (ie, the last dose of warfarin is given 6 days before surgery).[4,61] Normalization of the coagulation cascade may

Table 4. Summary of Recommended Perioperative Anticoagulation Management Strategies

Category	High bleeding risk procedure	Low bleeding risk procedure
High thromboembolic risk		
Warfarin	Give last dose 6 d before operation, bridge with LMWH or UFH, resume 24 h postoperatively.	Give last dose 6 d before operation, bridge with LMWH or UFH, resume 24 h postoperatively.
DOAC	Give last dose 3 d before operation,* resume 2 to 3 d postoperatively.	Give last dose 2 d before operation,* resume 24 h postoperatively.
Intermediate thromboembolic risk		
Warfarin	Give last dose 6 d before operation, determine need for bridging by clinician judgment and current evidence, resume 24 h postoperatively.	Give last dose 6 d before operation, determine need for bridging by clinician judgment and current evidence, resume 24 h postoperatively.
DOAC	Give last dose 3 days before operation,* resume 2 to 3 d postoperatively.	Give last dose 2 d before operation,* resume 24 h postoperatively.
Low thromboembolic risk		
Warfarin	Give last dose 6 d before operation, bridging not recommended, resume 24 h postoperatively.	Give last dose 6 d before operation, bridging not recommended, resume 24 h postoperatively.
DOAC	Give last dose 3 d before operation,* resume 2 to 3 d postoperatively.	Give last dose 2 d before operation,* resume 24 h postoperatively.

*In patients with CrCl < 50 mL/min on dabigatran, the last dose should be given 3 d before the procedure for low bleeding risk surgery, and 4 to 5 d before the procedure for high bleeding risk operation.
DOAC, direct oral anticoagulant; LMWH, low-molecular-weight heparin; UFH, unfractionated heparin.

take longer for elderly patients and patients with medical conditions that require anticoagulation to a higher INR level (standard therapeutic range is 2.0 to 3.0).[62,63] It is advisable to check the INR the day before the operation, if possible, to ensure that the patient's coagulation parameters are at a safe level.[61] If the INR is found to be supratherapeutic the day before the operation, prescribe oral vitamin K (1 to 2 mg) and recheck the INR the next day. On the day of the operation, intravenous vitamin K (single 1-mg dose) can be administered to normalize a patient's supratherapeutic INR.[64]

In terms of postoperative management, if deemed safe by the operating surgeon, warfarin should be resumed at previous dosing levels 12 to 24 hours after surgery.[4] Of note, the bioavailability of warfarin is strongly affected by the amount of vitamin K (decreases the anticoagulant effect) and vitamin E (increases the anticoagulant effect) in the diet, which often varies around an operative procedure. The patient's INR returns to a therapeutic level again in an average of 5 days.[4]

Direct oral anticoagulants

Several randomized controlled trials have demonstrated that DOACs can be safely managed in surgical patients, with bleeding and thrombosis rates that are noninferior to those with warfarin.[65] Although DOACs lack laboratory monitoring parameters and reversal agents (dabigatran is the exception), they are often favored over warfarin due to their shorter half-lives and more predictable pharmacology. Perioperative management strategies should be performed in a patient-centered manner, considering the bleeding risk of the surgery, the patient's renal function, and the agent's pharmacodynamics.[50] Procedures deemed to be low risk can be safely performed if <25% of the agent's anticoagulation effects are present, which requires withholding the DOAC for 24 hours in patients with normal renal function. For high risk procedures, <10% of the anticoagulant effect is considered safe, and this occurs once the DOAC is held for 48 hours in patients with normal renal function.[5,66]

Decisions around the timing of DOAC resumption postoperatively depend on the bleeding risk of the surgery, hemostasis, and individual patient risk factors. Caution should be exercised with post-procedural resumption due to their rapid onset (eg, peak plasma levels are reached in approximately 3 hours vs several days for warfarin). Resumption of DOACs perioperatively has not been prospectively studied, but in a large registry containing more than 2,000 patients undergoing mostly low bleeding risk surgery, DOAC resumption at 24 hours postoperatively was associated with a 1.2% (95% CI 0.6 to 2.1) 1-month major bleeding risk.[67] For high risk surgery or when hemostasis is in question, in practice, resumption is often delayed for 48 to 72 hours.

Antiplatelet agents

Management of perioperative antiplatelet therapy in patients with a significant cardiac history should be conducted in a multidisciplinary fashion, including input from the prescribing cardiologist, the anesthesiologist,

and the patient. As described in Section II, elective surgery should be deferred if possible for 14 days after balloon angioplasty, 30 days after bare-metal stent placement, and 1 year after drug-eluting stent placement. If a patient absolutely requires surgery less than 30 days out from drug-eluting stent placement, the American College of Cardiology (ACC) and American Heart Association (AHA) clinical practice guidelines recommend that dual antiplatelet therapy be continued if possible, and if not, aspirin should be continued and dual antiplatelet therapy should be resumed as soon as possible after surgery.[7]

Controversy exists over whether low-dose aspirin should be held in the perioperative period for major noncardiac surgery when it is prescribed for secondary prevention in patients with nonrecent (>4 to 6 weeks for bare-metal stent and >1 year for drug-eluting stent) history of cardiac stent placement. A recent meta-analysis that included 46 studies with more than 30,000 patients investigated the association of antiplatelet therapy with perioperative bleeding events in patients undergoing noncardiac surgery.[68] There was a minimal association between aspirin (relative risk [RR] 1.14; 95% CI 1.03 to 1.26, p = 0.009), and dual agent antiplatelet therapy (RR 1.33; 95% CI 1.15 to 1.55, p = 0.001) and the need for transfusion. The RR for bleeding requiring intervention, however, was not significantly different between antiplatelet therapy and control (aspirin had a RR of 0.96 [95% CI 0.76 to 1.22, p = 0.76], clopidogrel had a RR of 1.84 [95% CI 0.87 to 3.87, p = 0.11], and dual antiplatelet therapy had a RR of 1.51 [95% CI 0.92 to 2.49, p = 0.1]). Notably, a recently published randomized controlled trial called the PeriOperative Ischemic Evaluation-2 Trial (POISE-2) that was not included in the aforementioned meta-analysis found that patients at risk for vascular complications who received aspirin perioperatively were more likely to have a major bleeding event than those not on aspirin (hazard ratio 1.23; 95% CI 1.01 to 1.49), but found no differences between the groups in mortality or nonfatal myocardial infarction.[69] Therefore, we recommend holding aspirin (low/high dose) for 7 to 10 days before a high bleeding risk procedure in patients without history of percutaneous coronary intervention. Aspirin is rapidly absorbed by the stomach, and its inhibitive effect on platelets is evident within 1 hour. Given this, aspirin should not be restarted until the operative bleeding risk is minimal.[70] Clopidogrel, prasugrel, and ticagrelor therapy should be suspended for 5 to 7 days before low/high bleeding risk surgery.[4] Their onset of action is also within 1 hour, so considerations for restarting these agents are similar to aspirin.[70]

Section V: Considerations in the nonelective setting

Every surgeon should be prepared to manage antithrombotic therapy in patients who are actively bleeding or require nonelective surgery. Most antithrombotic agents can be reversed or at least mitigated by a reversal agent, antifibrinolytic, or blood product transfusion; DOACs are the notable exception. When formulating treatment decisions in emergency situations, one must weigh the risk of continued bleeding against the risk of clotting in the event that the antithrombotic agent is reversed and/or held. High-quality data in this area are lacking, and are based mostly on case series and expert consensus. Here we will outline and describe the effects of reversal agents and blood products that are useful for reversing the effects of antithrombotic agents, without proposing a management strategy guideline for emergency situations.

Nonoral anticoagulants

Unfractionated heparin (UFH) can be reversed effectively and completely with the administration of intravenous protamine. One milligram of protamine reverses 80 to 120 units of UFH; repeat dosages may be needed because UFH has a longer half-life (60 to 90 minutes) than protamine (approximately 7 minutes).

Protamine is widely used to reverse the effects of LMWH, but only has a partial effect.[71] No reversal agent exists for LMWH, but a new agent called ciraparantag has shown to safely and completely reverse LMWH in healthy volunteers, and is being further evaluated in a clinical trial (ClinicalTrials.gov: #NCT02207257).[72] Ciraparantag has been reported to antagonize the effects of all anticoagulants except for warfarin and argatroban. It is a synthetic molecule that forms hydrogen bonds to its intended targets and has been shown in pre-clinical studies to reverse the effects of heparin, fondaparinux, the factor Xa inhibitors (edoxaban, rivaroxaban, and apixaban), and dabigatran.[73]

Vitamin K antagonists

Vitamin K antagonists can be reversed by several treatment approaches: oral/parenteral vitamin K (phytonadione), prothrombin complex concentrates (PCCs), and fresh frozen plasma (FFP). Intravenous vitamin K should be administered in doses of 1 to 10 mg over a 30-minute infusion.[74] Prothrombin complex concentrates (KCentra; CSL Behring) is a low volume formulation of the clotting factors II, VII, IX, and X in an inactive form. It is administered intravenously in doses of 25 to 50 units/kg. Fresh frozen plasma contains the clotting factors II, VII, and X. Its utility in reversing INR is limited by its delayed onset,

the large volume required, and the inability to normalize INR below 1.6.[75] In a recently published randomized controlled trial, 4-factor prothrombin complex concentrate was demonstrated to be superior to fresh frozen plasma in reversing coagulopathy secondary to warfarin in patients requiring urgent surgery, where effective hemostasis was achieved in 78 (90%) patients in the 4-factor prothrombin complex concentrates group compared with 61 (75%) patients in the plasma group.[8] Therefore, we recommend the administration of vitamin K and 4-factor prothrombin complex concentrates to patients with an elevated INR secondary to warfarin who are actively bleeding and/or require urgent surgery.

Direct oral anticoagulants

Due to the rapid onset and short half-life of DOACs, patients clear the drug in 48 to 72 hours. In actively bleeding patients and/or those that require nonelective surgery, there are several strategies commonly used to reverse the effect of DOACs, none of which are nearly as effective as the 1 antidote currently available.

Dabigatran is the only DOAC with an antidote and the only DOAC that is effectively removed from the circulation through hemodialysis (factor Xa inhibitors are heavily protein-bound).[76] Idarucizumab (Praxbind; Boehringer Ingelheim Pharmaceuticals, Inc) is a monoclonal antibody that is FDA-approved for the reversal of dabigatran in the urgent and emergent surgical setting.[77] Idarucizumab, administered as a 1-time 5-gram dose via 5-minute IV infusion, results in immediate and sustained reversal of the effects of dabigatran.[9] The utility of idarucizumab is limited by its high cost; its wholesale cost was nearly $3,500 per patient dose in 2016.[78] We recommend administering idarucizumab to patients with evidence of significant dabigatran levels (by history of ingestion or laboratory parameter) who are bleeding or require emergency surgery.

There are several other DOAC reversal agents currently under development. Andexanet alfa (andeanet) is a recombinant modified human factor Xa decoy protein that is designed to neutralize the effects of factor Xa inhibitors (apixaban, edoxaban, enoxaparin, and rivaroxaban). It has been shown to be effective in reversing factor Xa inhibitors in phase I-III trials,[79] and a clinical trial is currently underway (Clinicaltrials.gov, #NCT02329327). As mentioned previously when discussing LMWH reversal agents, ciraparantag has also been demonstrated to be effective in reversing edoxaban in a clinical trial.[80]

Three small, randomized controlled studies in healthy volunteers found that 3-factor prothrombin complex concentrates (PCCs) reversed the anticoagulant effects of rivaroxaban and edoxaban.[10,11,13,81] In-vitro studies found 4-factor PCC to be superior to 3-factor PCC in correcting coagulation parameters.[12,82] Therefore, in certain emergency situations, 4-factor PCC transfusion (50 units/kg) is recommended for partial reversal in patients with evidence of active factor Xa inhibitors.

Antiplatelet agents

In bleeding patients and/or patients who require urgent or emergent surgery, platelet transfusion can replace the platelets whose function has been altered by antiplatelet agents, but there are very limited published data on the benefits/risks to platelet transfusion in this setting. Platelet function testing can help guide decision making by determining antiplatelet agents' current effect on circulating platelets, but is useful only in nonemergent situations.[83] In otherwise low-bleeding risk patients, surgeons usually operate without prophylactic platelet transfusion when aspirin is the only antiplatelet agent on board. One dose of platelets can be given preoperatively to patients on thienopyridine agents or dual agent antiplatelet therapy to reduce operative bleeding risk.[83] The standard recommended dose is 1 apheresed unit of platelets or 10 mL/kg of random-donor pooled platelet units. If an urgent clinical situation warrants preoperative platelet transfusion, we recommend transfusing 1 pooled unit of platelets immediately before surgery and redose as needed for ongoing bleeding.

DISCUSSION

These guidelines summarize the current evidence as well as guidelines previously endorsed by other groups to create a unique resource that surgeons can use to navigate the complicated, ever-changing topic of perioperative antithrombotic medication management. The most notable updates included here are the indications for heparin bridging, the perioperative management strategies for low-dose aspirin, as well as updated aspects of perioperative DOAC management. Heparin bridging is now recommended only for patients receiving warfarin who are considered high thromboembolic risk (CHA_2DS_2-VASc score ≥ 7, $CHADS_2$ score ≥ 5, mechanical heart valves, and VTE within 3 months). Perioperative continuation of low-dose aspirin in patients who have not undergone a percutaneous coronary intervention may cause more harm than benefit according to the recent POISE-2 trial. Finally, DOACs have emerged as a practical option for chronic anticoagulation that can be safely managed perioperatively. For the emergent setting, promising DOAC reversal strategies are in the late stages of development.

The value of multidisciplinary collaboration when making antithrombotic medication management decisions was emphasized here. Team-based care and consultation with

the physician who prescribed the antithrombotic agent are essential when making these decisions. Even more importantly, these management decisions should be made in a patient-centered manner, particularly in situations that require clarification through further research (eg heparin bridging, continuation vs discontinuation of low-dose aspirin used for secondary cardiovascular prevention).

When managing the antithrombotic medication in an individual patient, the perioperative antithrombotic medication strategy is determined by weighing the patient's thromboembolic risk if the antithrombotic is held against the patient's risk of perioperative bleeding if the antithrombotic is continued. To balance the risks, these guidelines described how to stratify perioperative thrombotic risk followed by procedural bleeding risk, heparin bridging considerations, and finally, how to create a perioperative antithrombotic medication management strategy for your next surgical patient. The final section briefly described antithrombotic agent reversal in emergent situations.

These guidelines are limited by the need for further research to provide further certainty and granulation to the findings discussed within. Our review noted many important areas in need of additional research, such as examining the utility of heparin bridging in patients who are high VTE risk. Another important identified area is determining procedural bleeding risk vs thrombotic risk if antithrombotic agents are continued. The default management strategy is to "be safe" and perioperatively hold medications that increase bleeding risk, so the uninterrupted administration of anticoagulants has not been thoroughly investigated for most surgical operations.

CONCLUSIONS

Patients prescribed chronic antithrombotic agents are increasingly encountered in surgical practice. These guidelines serve as a starting point for delivering evidence-based care and will be a useful resource for general surgeons. The evidence and processes contained herein can be incorporated into institutional pathways (standard operating procedures) and processes that assure high compliance across the phases of surgical care and among all individuals involved in surgical patient care, from front-line providers to hospital leadership. For more useful point-of-care information, ACS fellows have access to evidence-based practice guidelines on perioperative anticoagulation management as well as a wide range of surgical topics at http://ebds.facs.org.

Author Contributions

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eDocument 1. CASE VIGNETTES

A 77-year-old female with normal renal function and a $CHADS_2$ score of 5 takes dabigatran to prevent embolic complications resulting from nonvalvular atrial fibrillation. She presents to your clinic with an abnormal screening mammogram that requires a core needle biopsy. When should you instruct her to hold her dabigatran for the biopsy?

a. Hold dabigatran 5 days before the biopsy and prescribe therapeutic low molecular weight heparin for bridging.

b. Just perform the biopsy, no need to discontinue dabigatran.

c. Hold dabigatran for 2 days before the biopsy.

d. Hold dabigatran for 3 days before the biopsy.

The biopsy revealed invasive ductal carcinoma metastasized to the axillary lymph nodes and will require a modified radical mastectomy. When should you instruct her to hold dabigatran before surgery?

a. Hold dabigatran 5 days before the surgery and prescribe therapeutic low molecular weight heparin for bridging.

b. Just perform the surgery, no need to discontinue dabigatran.

c. Hold dabigatran for 2 days before the surgery, no need for heparin bridging.

d. Hold dabigatran for 3 days before the surgery, no need for heparin bridging.

A 56-year-old man with history of a mechanical mitral valve replacement 5 years ago on long-term warfarin therapy presents to your surgical clinic for a ventral hernia repair.

a. Stop warfarin 5 days before the administration, administer therapeutic-dose bridging with LMWH (1 mg/kg twice per day) preoperatively and postoperatively.

b. Reduce warfarin dose by 50% and instruct him to hold his dose on the day of surgery.

c. Continue warfarin without adjustment.

d. Stop warfarin 5 days before the operation and resume immediately after the operation, without heparin bridging.

Consider the same patient scenario except he takes long-term warfarin for secondary VTE prevention after getting a DVT during a flight to Hawaii last year.

a. Stop warfarin 5 days before the administration, administer therapeutic-dose bridging with LMWH (1 mg/kg twice per day) preoperatively and postoperatively.

b. Reduce warfarin dose by 50% and instruct him to hold his dose on the day of surgery.

c. Continue warfarin without adjustment.

d. Stop warfarin 5 days before the operation and resume immediately after the operation, without heparin bridging.