CHAPTER 9

Perioperative Anticoagulation

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INTRODUCTION

Deciding whether to discontinue or continue anticoagulation in patients prior to podiatric surgery can be difficult. The increased risk of thromboembolism must be weighed against the risk of bleeding and its complications in the intra- and postoperative period. This delicate balance is further complicated by the various anticoagulants being used such as antiplatelet agents, Vitamin K antagonists, direct oral anti-coagulants (DOAC), and heparins/low molecular weight heparins (LMWH). Antiplatelet therapy is also commonly seen and its management is one of the difficulties we face as podiatric physicians when determining if we can safely proceed with surgery. Although aspirin is seen more commonly on the preoperative medication list, many other antiplatelet therapies are seen especially in patients with peripheral vascular disease and those who have recently undergone vascular procedures. In this article, we will mainly focus on anticoagulants but will also give current recommendations with regard to antiplatelet therapy.

Many patient factors including heart valve prosthesis, atrial fibrillation, and patients who have recently undergone endovascular procedures have a bearing on the decision to continue (or when to restart) anticoagulation/antiplatelet therapy. Bridging is another topic that has been debated recently in the literature. Bridging is a viable option but only in select circumstances. Periprocedural management of patients receiving long-term oral anticoagulant therapy remains a common but difficult problem. Thromboembolic risk (although lacking in high-quality evidence) is the driving force where post-procedural bleeding determines when to resume therapy (1).

THROMBOEMBOLISM RISKS

The risk of thromboembolism includes both the continuation of anticoagulation therapy for thromboembolism and potential postoperative bleeding. Patients most at risk for thromboembolism include those with a history of thromboembolism, atrial fibrillation, and prosthetic heart valves (2). Patients with a history of a venous thromboembolism (VTE) and no history of hypercoagulable state or cancer see a significant decline in risk during the first month of anticoagulation therapy from 50% if no anticoagulation therapy is started to 10% while on anticoagulation. This risk decreases to 5% at the completion of 3 months. Long-term anticoagulation is usually reserved for those patients who have had multiple VTEs, and those with hereditary hypercoagulable states, or active cancer. In these patients, there remains approximately a 15% risk of VTE with discontinuation of oral anticoagulation (3).

The American College of Chest Physicians does not recommend routine blood testing with no familial history of hypercoagulable states in patients with their first DVT (4). Arterial embolism carries a significant risk especially in the elective surgery patient. In 2014, the American College of Cardiology and American Heart Association released guidelines on differentiating between patients with a <1% and >1% risk of cardiac complications. A tool for determining risk is the National Surgical Quality Improvement Program Myocardial Infraction and Cardiac Arrest (NQSIP MICA) score, which can be easily done online and is another tool to be used in conjunction with recommendations from the patient's cardiologist (5). Recurrent arterial thromboembolism can in many cases be associated with atrial fibrillation, which carries a different set of risks and recommendations (6) when it comes to interruption of anticoagulation therapy.

Atrial fibrillation (AF) and interruption of anticoagulation is difficult to classify because AF is often related to other cardiac diseases such as impaired left ventricular function, valve disease, and cardiac ischemia (7). Other variables that are associated with atrial fibrillation include age, hypertension, congestive heart failure, diabetes mellitus, history of stroke, and other vascular diseases (1). One method for predicting the risk of disrupting anticoagulation is the CHADS score (originally known as CHADS2, an updated version CHA2DS2-VASc is now available). This model takes into account patients who are receiving anticoagulation therapy for AF and the risk of stroke if therapy be discontinued. In the CHADS score, the letters correspond to disease states: C = congestive heart failure, H = hypertension, A = age (>75 years), D = diabetes mellitus, S = stroke (or prior thromboembolism), V = vascular disease, A = age (65-74 years), Sc = sex category (male/female). Each disease state is worth 1 point in the total score with the exception of those that are followed by a number with the number indicating the value in the score. Stroke risk increases from 0-15.2% with increasing score.

In addition, there have been multiple large-scale studies for comparison of warfarin versus LMWH and DOACs

(2). Knowledge of patients' risk factors can help in guiding the discussion with other health professionals in deciding whether or not to proceed with surgery based on the complete health profile of patients and aid in the decision of whether or not to interrupt anticoagulation therapy.

BRIDGING THERAPY

Bridging therapy consists of interruption of a long-acting anticoagulant and its replacement with a shorter-acting, (usually a heparin derivative), which can be discontinued either hours or up to a day prior to the surgery. The concerns associated with bridging are the possibility of rebound hypercoagulability once warfarin is resumed as well as increased biomarkers for hypercoagulability with abrupt cessation (8). Bridging was once a mainstay in anticoagulation treatment, but there have now been multiple studies that show major bleeding risks associated with bridging as well as the fact that the risk for developing thromboembolism is not significantly changed.

Bridging is now discouraged in a majority of patients and used mainly in those with a high risk of anticoagulation interruption. High risk patients include those who experienced a VTE with prior interruption of therapy, cerebrovascular accident or transient ischemic attack in the past three months, recent mural thrombus, mitral mechanical valve, VTE in the past 3 months, and history of VTE with known hypercoagulable state (9). Patients who are receiving DOACs or any form of heparin therapy do not require bridging. A large scale study examined the efficacy of bridging, and describing how bridging should be approached as follows: warfarin is stopped 5 days prior to the procedure with initiation of Dalteparin at 3 days prior to the procedure; this was interrupted 24 hours prior to the procedure taking place. Once the procedure was completed, Dalteparin was begun at 24 hours in patients at low risk and 48 hours in patients at high risk for bleeding, with Warfarin resuming 12 hours after the procedure or once the epidural catheter was removed. A significant risk of bleeding occurred in patients undergoing bridging without significant difference seen in the amount of thromboembolism postoperatively (10).

While bridging has been proven to be effective in high risk patients using both LMWH and DOACs, it is not recommended in the majority of surgical procedures and especially in those patients who are undergoing low-risk surgery. Patients who are receiving anticoagulants other than Warfarin must still be monitored, and the timing of cessation of anticoagulation to minimize both bleeding and thromboembolic risk is critical.

DISCONTINUATION OF DOAC THERAPY

DOAC therapy and the increasing use of non-vitamin K antagonist anticoagulation has simplified periprocedural anticoagulation management due its relatively short half-life and rapid onset of action with predictable pharmacokinetic properties (1). If the decision is made to discontinue anticoagulation therapy preoperatively, understanding the mechanism of action and the necessary amount of time needed before proceeding safely with surgery are important. Warfarin was discussed previously but in general, it needs to be discontinued 5 days prior to the procedure.

Dabigatrin is a direct thrombin inhibitor that reaches peak plasma concentration at 2 to 3 hours after intake. It has a relatively short half-life but needs to be discontinued for podiatric procedures 1 to 2 days prior to surgery in patients with a creatinine clearance of >50 ml/minute or 3 to 5 days prior to surgery in patients with a creatinine clearance <50 ml/minute.

Rivaroxaban is a direct factor Xa inhibitor that reaches peak plasma concentration in 2 to 4 hours after intake and should be discontinued at least 24 hours prior to surgical procedures.

Apixaban is also a direct factor Xa inhibitor with peak plasma concentrations reached at 1 to 4 hours after intake. It is recommended that Apixaban be discontinued at least 48 hours prior to a procedure with moderate to high risk of severe bleeding and at least 24 hours prior to a procedure with a low risk of significant bleeding.

Edoxaban also has a similar mechanism of action with direct Xa inhibition. Peak plasma concentration is seen at 1 to 2 hours. It is recommended that Edoxaban be discontinued 2 to 3 days prior to surgeries with a high bleeding risk and 24 hours prior to surgeries with a low bleeding risk (11).

DISCONTINUATION OF HEPARIN/ LMWH THERAPY

Heparin and the low molecular weight heparins have a similar mechanism of action but differ in the fact that Heparin affects thrombin (Factor IIa) and Factor Xa in a close to 1:1 ratio, as compared to LMWH, which affects Factor Xa and thrombin in a 4:1 ratio. In general Heparin is held from 4-6 hours prior to a procedure and has an immediate onset of action, while the dosing of LMWH and parenteral anticoagulants vary.

Agratroban in patients with normal hepatic function will need to be stopped 3 hours prior to the procedure. In those with decreased hepatic function, it is recommended

to stop at least 9 hours prior to procedure. The onset of anticoagulation is 30 minutes after the injection.

Bivalrudin in patients with creatinine clearance >30 ml/minute should be stopped 1.5 hours prior to surgery, and 3 hours prior to the procedure if the creatinine clearance is <30 ml/minute. The onset of action is 15 minutes after the injection.

Enoxaparin is slightly different and has both prophylactic dosing (stop 12 hours prior to the procedure start) and therapeutic dosing (stop at least 24 hours prior to the procedure). The onset of action is 3 to 5 hours after the injection.

Fondapurinux is similar to Bivalrudin in that creatinine clearance plays a role in discontinuation of therapy. If the creatinine clearance is >50 ml/minute, it will need to be stopped 3 days prior to the procedure. If the creatinine clearance is <50 ml/minute, it should be stopped 5 days prior to procedure. The onset of action is 3 hours after the injection (12).

DISCONTINUATION OF ANTIPLATELET THERAPY

Although only discussed briefly here, antiplatelet therapy is common in the podiatric patient population. At the author's hospital, the vast majority of patients who undergo arteriogram with vascular surgery are started on an antiplatelet regimen that includes both aspirin and clopidogrel, Aspirin is one of the most common drugs seen, especially in the geriatric population, when patients present for their preoperative evaluation. Platelet half-life plays a large role in the time needed to discontinue these medications because they are mostly irreversible inhibitors of platelets and therefore maximal effects and half-life of the drug correspond to the percentage platelets bound to the drug (12). Aspirin is the outlier in this group in terms of mechanism of action because it works by irreversible inhibition of both COX-1 and COX-2 inhibitors whereas the rest of the antiplatelet medications works by irreversible inhibition of P2Y12ADP receptor (involved in platelet aggregation).

Aspirin has a short interim to maximum level of only 30 to 40 minutes, it does however persist for at least 4 days and recommendations vary depending on the surgical risk, and range from continuation of therapy if there is a high risk, 4 days if moderate risk, and 7 to 10 days if there is a low risk of adverse cardiac event with discontinuation of therapy (12,13).

Clopidogrel irreversible P2Y12ADP inhibitor has a time to maximum level of 1 hour for the circulating drug and up to 7 days for maximal antiplatelet effect. Effects on circulating platelets are present for up to 10 days, and current recommendations are discontinuation of therapy 5 days prior to the procedure.

Ticragrelor is similar to clopidogrel in that it is a P2Y12ADP inhibitor, it has a time to maximum effect of 1.5 hours, and the residual antiplatelet effect is down to 30% after 2.5 days with a recommendation to discontinue the medication 5 days before scheduled procedures.

Cilostazol an inhibitor of phosphodiesterase III and has current recommendations of stopping therapy only 1 to 2 days prior to the procedure (12).

In conclusion, most of the anticoagulation and information posted here can be found through thorough discussion with the patient's cardiologist and primary caregivers. However, it is important to be aware of the risks we are undertaking when going into surgery because the final decision for whether or not to proceed with surgery ultimately lies with the podiatric surgeon who is taking the patient to the operating room. Inpatient podiatric surgery is commonly preceded by endovascular intervention for optimization of blood flow and requests are made to hold or continue anticoagulation/antiplatelet therapy. Hopefully this guide can serve as a basis for discussion with other specialists to optimize patient health and safety prior to surgery.

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