



Anticoagulation Management in Geriatric Orthopedic Trauma Patients

Jensa C. Morris¹ · Mary I. O'Connor²

Accepted: 28 October 2020 / Published online: 18 November 2020
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Abstract

Purpose of Review This article will review the perioperative management of geriatric patients on anticoagulants who present for non-elective orthopedic surgery.

Recent Findings Our understanding of best practices in perioperative anticoagulation management has advanced significantly over the last 5 years. More patients are presenting for surgery on direct oral anticoagulants which require a different approach than the vitamin K antagonist, warfarin. We have come to better appreciate the importance of time to the operating room on outcomes, specifically in hip fracture surgery. Regional anesthesia now has standardized guidelines for preprocedure anticoagulation interruption. Prothrombin complex concentrate has increasing acceptance for warfarin reversal preoperatively. Reversal agents are now available for the direct oral anticoagulants but are not recommended for standard use preprocedure. And there has been a shift away from routine use of bridging anticoagulation preprocedure.

Summary A team-based approach with input from the surgical, anesthesia, and internal medicine or geriatric team preoperatively is critical to the management of perioperative anticoagulation.

Keywords Geriatric · Anticoagulation · Hip fracture surgery · Trauma · Perioperative care · Atrial fibrillation

Introduction

The challenge addressed by this article is the management of a patient on therapeutic anticoagulation who requires urgent or emergent orthopedic surgery. We will discuss perioperative management of commonly used anticoagulants in the outpatient setting including the vitamin K antagonist, warfarin, and the direct oral anticoagulants (DOAC), rivaroxaban, apixaban, edoxaban, and dabigatran. As injectable agents are not commonly prescribed for long-term therapy in outpatients, low molecular weight heparin and fondaparinux will not be addressed. Prevention of venous thromboembolism postoperatively is a review unto itself and will not be discussed here.

Furthermore, the perioperative management of antiplatelet agents such as aspirin, clopidogrel, and ticagrelor is out of the scope of this review.

The term anticoagulation will refer to full, therapeutic anticoagulation used to treat venous thromboembolism or prevent stroke in patients with mechanical valves or atrial fibrillation. Lower doses of anticoagulation used to prevent blood clots will be differentiated with the term DVT prophylaxis. Anticoagulation includes warfarin dosed to a target INR of 2–3 or treatment with a full dose DOAC agent, dose-adjusted as necessary for renal function.

Perioperative management of anticoagulation will be discussed as pertaining to urgent surgical procedures and not elective surgeries. Patients undergoing elective orthopedic surgery are evaluated preoperatively by their primary care physician or cardiologist with the goal of establishing a perioperative anticoagulation plan prior to surgical admission. Most perioperative anticoagulation plans utilize standardized protocols based on the prescribed anticoagulant and the estimated surgical bleeding risk. Hip fracture surgery will be used as the primary example of urgent orthopedic surgery in the geriatric patient on anticoagulation but the principles can be applied more broadly to geriatric orthopedic trauma.

This article is part of the Topical Collection on *Geriatric Orthopedics*

✉ Jensa C. Morris
jensa.morris@ynhh.org

¹ Hospitalist Service, Yale New Haven Hospital, 20 York Street, New Haven, CT 06510, USA

² Department of Orthopaedics & Rehabilitation, Yale University, New Haven, USA

Background

As the population continues to age, we are seeing an increase in geriatric trauma. A recent study reported that 25% of all orthopedic trauma patients were > 65 years old, most suffering from ground-level falls [1]. Anticoagulant use is common among patients undergoing orthopedic surgery and, specifically, hip fracture surgery. A 2017 study of geriatric trauma patients in Florida reported that 42% of patients admitted were on anticoagulants or antiplatelet agents. Of those patients prescribed preoperative anticoagulation or antiplatelet agents, 16.5% were anticoagulated with warfarin and 1% with DOACs [2]. This corresponds with a 2011 Medicare data set showed that 12.8% of Medicare patients were prescribed vitamin K antagonist treatment [3].

Anticoagulant use has the potential to delay surgical treatment. One study demonstrated that hip fracture patients on warfarin had a significant delay to OR beyond 48 h with an associated increase in 30-day, 3-month, and 1-year mortality as compared to patients on no anticoagulation [4]. Decisive management of anticoagulation is essential to optimize patient safety and expedite urgent surgery. In the case of hip fracture surgery, it is well established that mortality increases with time to the operating room greater than 24 h [5].

Urgency of Procedure

When evaluating an anticoagulated orthopedic patient for surgery, it is critical to determine the urgency of the surgical procedure. The risk associated with delaying operative care is surgery specific: Patients with an orthopedic emergency such as a long bone fracture with acute compartment syndrome will have minimal time for anticoagulation reversal if emergent operative intervention is required. Hip fracture surgery is considered urgent but not emergent based on known mortality increase with operative delay greater than 24 h [5, 6]. In contrast, any surgical procedure that can be safely delayed beyond 48–72 h without any impact on clinical outcome is considered non-urgent and allows for complete reversal of anticoagulation, similar to an elective procedure.

Procedure Bleeding Risk

In determining a safe perioperative anticoagulation plan, understanding the risk of surgical bleeding is essential. Orthopedic surgery has largely been classified as high bleeding risk except hand surgery and arthroscopic surgery. However, most would agree that there is significant variation in expected blood loss within each surgical category. For example, hip fracture surgery may have an expected blood loss of < 50 cc in a percutaneous pinning, while a hip fracture requiring a total hip arthroplasty or revision arthroplasty surgery may have significantly more predicted blood loss.

In addition to estimating procedure-specific bleeding risk, we need to consider the consequences of surgical bleeding. Uncontrolled continuous operative bleeding can obscure the surgical field, increase operative time, and increase the risk of anesthetic and hemodynamic consequences. Patients with increased operative blood loss are more likely to require an allogenic blood transfusion. Allogenic blood transfusion exposure significantly increases the risk of surgical site infection as demonstrated in multiple studies of total hip and knee arthroplasty [7]. Poor hemostasis with postoperative hematoma formation at the surgical site is a well-established risk factor for infection [8]. The human and financial cost of a surgical site infection is high. Patients with SSI are 60% more likely to require ICU admission, five times more likely to be readmitted, have three times the hospital stay duration, and a mortality rate five times higher than in patients without wound infections [9]. Furthermore, the site of bleeding is essential to consider. Bleeding into an expansible thigh after hip fracture surgery has far less clinical significance than epidural bleeding after spine surgery. The operating surgeon is best positioned to estimate anticipated procedure blood loss and discuss preoperative anticoagulation targets specific to the procedure.

Anesthetic Considerations

The type of anesthesia planned is critical to consider in making anticoagulation recommendations. In 2018, the American Society of Regional Anesthesia released their most recent guidelines on timing of regional anesthesia in patients receiving antithrombotic therapy [10]. Spinal hematoma is a rare but potentially catastrophic complication of neuraxial anesthesia. Horlocker et al. estimate the risk of hematoma to be approximately 1 in 150,000 epidural and 1 in 220,000 spinal anesthetics in patients on no anticoagulation or DVT prophylaxis alone [11]. The authors point out that in the absence of a central reporting system, this may be a significant underestimation. An analysis of the American Society of Anesthesiologists Closed Claims database over a 19-year period reported legal claims related to 36 spinal hematomas. Of these, 75% had evidence of preexisting or iatrogenic hemostatic abnormalities. As a result, our anesthesia colleagues strictly adhere to guideline-directed management of anticoagulant agents prior to neuraxial and regional anesthesia. The most recent guidelines are available as a mobile application [12]. The application is designed to allow easy access to ASRA guidelines on anticoagulant interruption pre- and post-anesthetic procedures. This technology has allowed internists, surgeons, and anesthesiologists to communicate clearly regarding anticoagulation management before and after neuraxial anesthesia.

No specific anticoagulation precautions are required prior to general anesthesia. General anesthesia must be the default option for patients who require urgent or emergent surgery

and are currently taking anticoagulation that cannot be fully reversed prior to the procedure. Discussion with the anesthesia team to determine the preferred and any alternative anesthetic modality will assist in determining the timing of the procedure and need for anticoagulant reversal.

Anticoagulant Agent

The anticoagulant agent itself and patient factors affecting metabolism of that agent are critical to carefully assess. Define which agent the patient is taking and the timing of the patient's most recent dose. It is surprising how often we see the DOACs interchanged in the charts with inaccurate reporting of which agent the patient is prescribed and when the last dose was taken. Each agent has unique pharmacology, pharmacokinetics, drug interactions, lab monitoring, and options for reversal.

Of the oral anticoagulants, the vitamin K antagonist, warfarin, reduces circulating levels of coagulation factors II, VII, IX, and X. Warfarin has a slow onset of action with peak effect at 48 h and duration of activity of up to 5 days. Effect is variable with both genetic and environmental factors affecting individual drug response. Anticoagulant effect of warfarin is assessed with INR monitoring.

Dabigatran directly inhibits thrombin; rivaroxaban, apixaban, and edoxaban directly inhibit factor Xa. Together, these agents are categorized as the direct oral anticoagulants (DOACs). DOACs have a rapid onset of action with peak effect 2 to 4 h following oral administration. They have predictable anticoagulant and pharmacodynamic effects with minimal drug interactions. In contrast to warfarin, there is no requirement at present for lab monitoring of the anticoagulant intensity of the DOACs. Overall, when compared to warfarin, DOACs have a lower risk for intracranial bleeding and other types of minor and major bleeding [13–15]. In the absence of contraindications or financial constraints, these agents are now favored over warfarin for long-term outpatient use.

The half-life of the oral anticoagulant will determine residual anticoagulant effect at the time of surgery. The patient's renal function as measured by creatinine clearance contributes in large part to the medication half-life. Based on the principle that in four to five half-lives, a medication will be entirely eliminated, general consensus is that high bleeding risk surgery may be completed after four half-lives have elapsed. Low to intermediate bleeding risk surgery, in which residual anticoagulant effect is acceptable, may be done after two half-lives have elapsed from the last dose. Very low bleeding risk procedures may be done without delay. This is illustrated in Table 1.

Estimating anticoagulant half-life is largely dependent on renal clearance but can also be impacted by drug interactions. Amiodarone, diltiazem, and verapamil are all commonly used in patients with atrial fibrillation and can all affect anticoagulant drug levels. Amiodarone inhibits CYP3A4 and P-gp and is associated with increased levels of dabigatran and rivaroxaban when used concurrently. Diltiazem and verapamil are both weak to moderate inhibitors of CYP3A4 and substrates for P-gp. Concurrent use of dabigatran and verapamil leads to elevated dabigatran drug levels. Elevations in rivaroxaban levels are also seen with concurrent use of diltiazem. These drug-drug interactions are more pronounced in the setting of renal insufficiency and therefore often become relevant during acute illness and the perioperative period.

Sample Preoperative Anticoagulation Protocol

At our institution, we have categorized hip fracture surgery by the anticipated blood loss of the planned procedure. Percutaneous pinning is considered very low bleeding risk and can be performed without delay in patients on DOACs or on warfarin with INR < 3.0. Estimated bleeding risk of hip fracture surgery procedures is shown in Table 2. Certainly, one could argue the categorizations, but this was a classification scheme that our surgeons agreed to use as guidance. Once

Table 1 Recommended time of discontinuation of direct oral anticoagulants (DOACs) prior to surgery

| Direct oral anticoagulant | Creatinine clearance (ml/min) | Half-life (hours) | Very low bleeding risk procedure | Low to intermediate bleeding risk procedure | High bleeding risk procedure |
|---------------------------|-------------------------------|-------------------|----------------------------------|---|------------------------------|
| Dabigatran | > 50 | 13–15 | No delay | 1 day | 2 days |
| | 30–50 | 18 | | 2 days | 4 days |
| | < 30 | 27 | | 2–5 days | >5 days |
| Rivaroxaban | > 50 | 8–9 | No delay | 1 day | 2 days |
| | 30–50 | 9 | | 1 day | 2 days |
| | 15–30 | 8–10 | | 2 days | 3 days |
| Apixaban | > 50 | 12 | No delay | 1 day | 2 days |
| | 30–50 | 17–18 | | 2 days | 3 days |
| | 15–30 | 17–18 | | 2 days | 3 days |

[16]

Table 2 Hip fracture surgery estimated bleeding risk

| Surgical procedure | Expected blood loss | Hip fracture surgery bleeding risk |
|--|---------------------|------------------------------------|
| Percutaneous pinning | < 50 cc | Low |
| Compression hip screw with side plate Short intramedullary nail without reaming | 50–100 cc | Intermediate |
| Hemiarthroplasty Long intramedullary nail with reaming | 100–200 cc | Higher |
| Periprosthetic fracture | | |
| Pathologic fracture | | |

the bleeding risk category has been defined, the time to OR is determined by the specific anticoagulant agent and creatinine clearance. This is shown in Table 3.

For example, a patient on warfarin with an INR of 2.9 undergoing a percutaneous pinning may proceed to the OR without delay. A patient on apixaban with creatinine clearance > 60 ml/min who received the last dose on Monday morning at 8 am may undergo intramedullary hip screw placement on Tuesday morning. However, if that same patient had acute kidney injury with creatinine clearance < 30 ml/min on admission, it would be important to consider surgical delay to Wednesday morning, weighing carefully bleeding risk with risk of operative delay.

Sample Hip Fracture Anticoagulant Management Protocol

Reversal Options

Patients admitted on anticoagulation who require urgent or emergent surgery will need to be evaluated for possible reversal of anticoagulation. Patients on warfarin can be treated with vitamin K with an expectation of partial reversal at 12 h. The full effect of vitamin K reversal may not be seen until 24 h after administration. Vitamin K may be administered orally, intravenously, or subcutaneously. As these surgical patients will require resumption of warfarin anticoagulation postoperatively, vitamin K should be given at a dose that will lower the INR to a safe range but will not cause resistance to anticoagulation postoperatively. For this reason, we recommend vitamin K 2.5 mg orally once (see Fig. 1).

Vitamin K is rarely used as the sole reversal agent for warfarin in patients hospitalized with the need for urgent surgery. Traditionally, fresh frozen plasma (FFP) has been used to supplement vitamin K. The disadvantages of FFP administration include volume of blood product required, incomplete reversal of INR, and short duration of action of 6–8 h with rapid dissipation of effect. As with any blood product, there is a risk of allergic reaction and anaphylaxis, transmission of infection, and transfusion-associated circulatory overload.

The timing of FFP dosing is important and can be cumbersome to coordinate. FFP is administered at a dose of 12–15 ml/kg. Each unit has an approximate volume of 270–320 ml. For example, a 70-kg patient should receive 4 U of FFP based on $(70 \text{ kg} \times 15 \text{ ml/kg})/270 \text{ ml/U} = 3.9 \text{ U}$. Each unit requires 20–30 min to thaw and should be administered as soon as possible after thawing. Each unit should be given over 20–30 min. When coordinating an urgent surgery that is often scheduled in an “add-on” position without a clear OR start time, it can be complicated to ensure that FFP is administered prior to incision but not too early that the effect has dissipated.

Another warfarin reversal option is prothrombin complex concentrate (PCC). PCC is a pooled plasma product comprised of factors II, VII, IX, and X. It is administered as a weight-based dose reconstituted in 20 mL of diluent and infused over 10 min. Peak effect of PCC is achieved at 10–30 min after administration with ongoing efficacy 24–48 h post-infusion [17]. Unlike FFP, PCC does not require blood group typing or thawing. Advantages of PCC include rapid reversal of coagulopathy, low risk of viral transmission, low risk of allergic reaction, decreased total volume of infusion, and weight-based dosing [18]. The most common side effect of PCC is headache. No difference in thromboembolic risk has been seen with PCC use as compared with FFP [19]. Despite the clear advantages of PCC over FFP, many hospitals restrict the use of PCC due to the significant increase in cost as compared with FFP.

The direct oral anticoagulants rivaroxaban, apixaban, and dabigatran have FDA-approved specific reversal agents. Idarucizumab is a monoclonal antibody that binds directly to thrombin with greater affinity than dabigatran. Maximum reversal of the anticoagulation effect of dabigatran occurs at 4 h after treatment. Andexanet alfa is a recombinant modified factor Xa protein that acts as a “decoy,” causing the DOACs apixaban and rivaroxaban to bind to it instead of natural factor Xa. Both idarucizumab and andexanet are associated with increased thromboembolic events. Use is therefore limited to patients experiencing life-threatening bleeds. We do not recommend the use of idarucizumab or andexanet for routine preoperative anticoagulation reversal.

Table 3 Recommended operative timing

| Anticoagulant agent | Hip fracture surgery bleeding risk | Creatinine clearance | Time/criteria for OR* |
|------------------------------|------------------------------------|----------------------|-----------------------|
| Warfarin (Coumadin) | Low | Any | INR < 3 |
| | Intermediate | Any | INR < 2 |
| | High | Any | INR < 2 |
| Direct oral anticoagulants** | Low | CrCl > 50 ml/min | No delay |
| | | CrCl 30–50 ml/min | No delay |
| | | CrCl < 30 ml/min | No delay |
| | Intermediate | CrCl > 50 ml/min | 24 h |
| | | CrCl 30–50 ml/min | 48 h |
| | | CrCl < 30 ml/min | 48 h |
| | High | CrCl > 50 ml/min | 48 h |
| | | CrCl 30–50 ml/min | 72 h |
| | | CrCl < 30 ml/min | 72 h |

*Surgeon may opt to operate earlier if clinical factors suggest lower bleeding risk or a higher complication risk associated with delay to OR. Note that time to OR is determined by INR in the case of warfarin and by timing of last dose and creatinine clearance in the case of the DOACs

**Rivaroxaban (Xarelto), apixaban (Eliquis), dabigatran (Pradaxa)

Prior to the availability of specific antidotes to DOACs, PCC was utilized as an emergency reversal agent. In patients on DOAC therapy, PCC effectively achieves hemostasis in the setting of major hemorrhage 66 to 95% of the time based on low-quality studies [20, 21]. PCC has not been well studied for reversal of DOAC therapy in the perioperative setting. There are legal and ethical questions regarding the use of PCC for DOAC reversal given that there are now FDA-approved reversal agents. PCC is recommended as an option for warfarin reversal but not DOAC reversal preoperatively.

Given that there is no clear pathway for preoperative reversal of DOAC anticoagulant effect in the absence of major hemorrhage, other options should be considered. Within our hip fracture program, we have prioritized reducing time to the

OR. In coordination with the surgical team, we have set aggressive time to OR targets in anticoagulated patients with hip fractures. Within this protocol, patients on DOACs undergoing only the highest bleeding risk procedures or with significant renal insufficiency may require a 48-h delay to OR (Tables 2 and 3).

Bridging Anticoagulation

After determining the timing of the operative procedure, the next question to address is if bridging anticoagulation is required. This is determined by the patient's indication for anticoagulation and their most recent thrombotic event as this will determine the risk associated with anticoagulation

Fig. 1 Sample warfarin reversal protocol. The asterisk indicates INR target determined by surgical procedure. PCC, prothrombin complex concentrate; INR, international normalized ratio; FFP, fresh frozen plasma

SAMPLE WARFARIN REVERSAL PROTOCOL:

- Stop warfarin on admission
- If INR > target,* administer vitamin K 2.5 mg orally x 1 immediately
- Initiate routine DVT prophylaxis
- Recheck INR morning of surgery
- If INR still > target, administer Prothrombin Complex Concentrate (PCC, K-Centra) prior to OR
 - PCC dose is calculated using patient weight and pretreatment INR
 - Onset of action of PCC is within 10 minutes. No delay required after administration of PCC and surgery onset.
 - Duration of action of PCC is 24–48 hours.
- Fresh frozen plasma may be given if PCC is not available.
 - Total dose of FFP should be calculated as 15 ml/kg
 - Each unit of FFP is approximately 250 cc
 - FFP requires 20–30 minutes to thaw. Each unit of FFP is infused over 30–60 minutes
 - FFP should not be given more than 6 hours prior to surgery
 - FFP should be avoided in patients at risk of volume overload

*INR target determined by surgical procedure.

PCC, prothrombin complex concentrate; INR, international normalized ratio; FFP, fresh frozen plasma

interruption. For example, a patient with pulmonary embolus within the last 3 months is at much higher risk for thrombotic complication than a patient with recurrent venous thromboembolic disease on chronic anticoagulation with no events in many years.

The most common indication for anticoagulation in geriatric orthopedic patients is atrial fibrillation. The incidence of atrial fibrillation on admission in patients referred to the hospital for hip fracture has been reported to be between 7 and 10% [22, 23]. The challenge is to determine when the risk of thrombosis from anticoagulation interruption outweighs the risk of surgical bleeding associated with anticoagulation continuation.

The risk of thrombotic complications perioperatively in patients with atrial fibrillation may be assessed using the CHADS2 or CHADS2VASC score. These scores were originally developed to assist clinicians in better assessing stroke risk in clinically stable outpatients with atrial fibrillation. The scores account for comorbidities including congestive heart failure, hypertension, age 75 years or older, diabetes mellitus, and history of stroke or transient ischemic attack. The CHADS2 and CHADS2VASC scores have not been prospectively validated as predictors of postoperative stroke. Nonetheless, these scores can be helpful in the perioperative period. The BRIDGE trial, published in the *New England Journal* in 2015, evaluated the risk of postoperative arterial thromboembolism in patients with atrial fibrillation. Patients were randomized to receive bridging anticoagulation with low molecular weight heparin or placebo during warfarin interruption perioperatively. There was no reduction in the incidence of arterial thromboembolism with bridging therapy. There was, however, a more than 2-fold increase in incidence of major bleeding [24]. This study has transformed our thinking on perioperative anticoagulation management. We now understand that patients with atrial fibrillation rarely require full therapeutic anticoagulation bridging therapy during interruption of their home anticoagulant agents.

There may be a few exceptions to this rule. Patients in the BRIDGE trial had an average CHADS2 score of 2.3 with few patients scoring 5 or 6 on this scale. From this study, we cannot conclude that bridging anticoagulation is either helpful or harmful in this highest thrombotic risk group. The American College of Chest Physicians (ACCP) guidelines

on this were last updated in 2012 and do not include the BRIDGE trial. These guidelines favor bridging anticoagulation for patients with atrial fibrillation with an elevated CHADS2 score; any history of stroke or transient ischemic attack; and a low CHADS2 score (< 5) but with a history of arterial thromboembolic event with temporary interruption in anticoagulation [25]. These guidelines are due to be updated.

Based on the current literature, we recommend restricted use of bridging anticoagulation. Only patients at the highest risk of thrombotic complications receive full therapeutic dose bridging anticoagulation with low molecular weight heparin or unfractionated heparin. Other examples of very high thrombotic risk conditions include older mechanical valves or any mitral mechanical valve or arterial or venous thromboembolism within the last 3 months. The highest risk patient groups are outlined in Table 4. In our practice, there has been a distinct paradigm shift from using bridging anticoagulation routinely to using it rarely and only with a compelling indication.

Inferior Vena Cava Filter

There are very limited indications for inferior vena cava (IVC) filter placement in the perioperative period. Patients with an acute venous thromboembolic event within the last 3 months who require anticoagulation interruption for surgery may be considered for IVC filter placement preoperatively [26–28]. In the absence of a recent high-risk thrombotic event, there are no data to support IVC filter placement prophylactically prior to surgery in patients who cannot be anticoagulated. In one study, IVC filters were associated with a 4% procedural complication rate and a 17% complication rate in the month post-placement. Only just over a third of filters were retrieved as indicated at 19 weeks of follow-up [29]. In our practice, we almost never recommend IVC filter placement prior to hip fracture surgery.

Postoperative Resumption of Anticoagulation

Timing of anticoagulation resumption postoperatively can be contentious and potentially confusing. There is little evidence to guide decision-making here. We recommend that full therapeutic anticoagulation resume as soon as

Table 4 Thromboembolic risk and recommendation for bridging anticoagulation

| Thromboembolic risk | Mechanical valve | Atrial fibrillation | Arterial or venous thromboembolism | Recommendation |
|---------------------|---|---------------------|---|------------------------------------|
| Higher | Any mitral prosthesis Older mechanical valve (caged ball, tilting disk) | CHADS2 \geq 5 | Recent (\leq 3 months) thromboembolism | Consider bridging anticoagulation* |
| Lower | Bileaflet aortic valve | CHADS2 0–4 | Thromboembolism > 3 months prior | No bridging anticoagulation |

*Bridging anticoagulation may not be favored if anticipated interruption is < 3–5 days, concurrent dual antiplatelet therapy, active bleeding, high risk of major bleeding, no prior thromboembolism, atrial fibrillation patient in sinus rhythm

possible postoperatively. We resume full dose anticoagulation 24 h after hip fracture surgery as long as routine hemostasis has been achieved. The DOACs may be resumed on postoperative day 1 and will be expected to achieve therapeutic effect within 2–4 h. Warfarin, however, does not achieve peak effect for up to 4 days from initiation. A common error is to resume warfarin immediately postoperatively with the intent of allowing the INR to safely “drift” upward to therapeutic range. This is dangerous in that it leaves to patient unprotected from postoperative VTE and at risk of arterial or venous thrombosis related to the condition for which the warfarin was originally prescribed. When warfarin is resumed postoperatively, full therapeutic anticoagulation by an alternative means (usually low molecular weight heparin) is required until INR is within the patient’s target therapeutic range.

Discussion with the surgical team regarding risks of rapid vs. delayed resumption of anticoagulation is important to balance surgical and medical perioperative risks and to establish trust among the treating teams. An essential point to remember is that while age and comorbidities increase the risk of bleeding on anticoagulation [30], the very same factors increase risk of postoperative thromboembolic events. Bleeding risk on anticoagulation increases from 2.9% per year in patients under age 85 to 4.0% per year in patients 85 years and older. Thromboembolic complications disproportionately increase from 2.8 to 6.3% in the same age categories [31]. In general, the net clinical benefit favors prompt resumption of anticoagulation postoperatively. The conversation with the surgical team might include a discussion of staggered resumption of antiplatelet and anticoagulant medications to mitigate bleeding risk and contingency plans to address potential complications such as prolonged wound drainage.

Conclusion

Perioperative anticoagulation management is a prime example of the importance of team-based perioperative care. There is no substitute for a conversation with the physician prescribing the anticoagulation to determine the risk of interruption; discussion with the anesthesia team on the impact of anticoagulation on the planned anesthetic modality; and discussion with the surgeon regarding procedure-specific bleeding risks. Involvement of hospital pharmacists can be useful in determining access to reversal agents, dose-adjustments for renal insufficiency, and concerning drug-drug interactions that might impact anticoagulant duration of action. Clear hospital or program-level guidelines on perioperative anticoagulation should be in place to guide these conversations and allow for consistent decision making.

Compliance with Ethical Standards

Conflict of Interest The authors have no financial conflicts of interest to disclose.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

References

- Peterson BE, Jiwanlal A, Della Rocca GJ, Crist BD. Orthopedic trauma and aging: it isn’t just about mortality. *Geriatric Orthop Surg Rehab*. 2015;6(1):33–6.
- Ang D, Kurek S, McKenney M, Norwood S, Kimbrell B, Barquist E, et al. Outcomes of geriatric trauma patients on preinjury anticoagulation: a multicenter study. *Am Surg*. 2017;83:527–35.
- Dossett LA, Riesel JN, Griffin MR, Cotton BA. Prevalence and implications of preinjury warfarin use: an analysis of the National Trauma Databank. *Arch Surg*. 2011;146:565–70.
- Caruso, G, Andreotti M, Tonon F, Corradi N, Rizzato D, Valentini A, Valpiani G, Massari L. The impact of warfarin on operative delay and 1-year mortality in elderly patients with hip fracture: a retrospective observational study. *J Orthop Surg Res*. 2019;14(169). <https://doi.org/10.1186/s13018-019-1199-5>.
- Pincus D, Bheeshma R, Wasserstein D, Huang A, Paterson JM, Nathens AB, et al. Association between wait time and 30-day mortality in adults undergoing hip fracture surgery. *JAMA*. 2017;318(20):1994–2003.
- Morrissey N, Iliopoulos E, Osmani AW, Newman K. Neck of femur fractures in the elderly: does every hour to surgery count. *Injury. Int J Care Injured*. 48:1155–8.
- Kim JL, Park JH, Han SB, Cho IY, Jang KM. Allogenic blood transfusion is a significant risk factor for surgical site infection following total hip and knee arthroplasty: a meta-analysis.
- Parvizi J, Azzam K, Rothman RH. Deep venous thrombosis prophylaxis for total joint arthroplasty: American Academy of Orthopaedic Surgeons guidelines. *J Arthroplast*. 2008;23(7 Suppl):2–5.
- Wellisz T. Management of bone bleeding during surgery and its impact on the incidence of post-operative osteomyelitis, osteomyelitis. In: Baptista, MS, Tardivo JP (eds) *IntechOpen*. 2012. <https://doi.org/10.5772/31623>
- Horlocker TT, Vandermeulen E, Kopp SL, Gogarten W, Leffert LR, HT. Regional anesthesia in the patient receiving antithrombotic or thrombolytic therapy. American Society of Regional Anesthesia and Pain Medicine evidence-based guidelines (fourth edition). *Reg Anesth Pain Med*. 2018;43:263–309.
- Horlocker TT, Wedel DJ. Anticoagulation and neuraxial block: historical perspective, anesthetic implications, and risk management. *Reg Anesth Pain Med*. 1998;23:129–34.
- ASRA (2018) ASRA Coags 2.1 [Mobile application software]. Retrieved from <http://itunes.apple.com>.
- Connolly SJ, Ezekowitz MD, Yusuf S, et al. RE-LY Steering Committee and Investigators. Dabigatran versus warfarin in patients with atrial fibrillation. *N Engl J Med*. 2009;361(27):1139–51.
- Patel MR, Mahaffey KW, Garg J, et al. ROCKET AF Investigators. Rivaroxaban versus warfarin in nonvalvular atrial fibrillation. *N Engl J Med*. 2011;365(10):883–91.
- Granger CB, Alexander JH, McMurray JJV, et al. ARISTOTLE Committees and Investigators. Apixaban versus warfarin in patients with atrial fibrillation. *N Engl J Med*. 2011;365(11):981–92.

16. Anderson M, Hassell K, Trujillo T, Wolfe B. When patients on target-specific oral anticoagulants need surgery. *Cleve Clin J Med*. 2014;81:629–39.
17. Pabinger I, Brenner B, Kalina U, Knaub S, Nagy A, Ostermann H. Prothrombin complex concentrate (Beriplex P/N) for emergency anticoagulation reversal: a prospective multinational clinical trial. *J Thromb Haemost*. 2008; 6 (4):XXXX.
18. Burk DR, Smith JL, Wild J. Prothrombin complex concentrates: an alternative to fresh frozen plasma. *Orthopedics*. 2017;40(2):e367–9.
19. Levy JH, Douketis J, Steiner T, Goldstein JN, Milling TJ. Prothrombin complex concentrates for perioperative vitamin K antagonist and non-vitamin K anticoagulant reversal. *Anesthesiology*. 2018;129(6):1171–84.
20. Tao J, Bukanova EN, Akhtar S. Safety of 4-factor prothrombin complex concentrate (4F-PCC) for emergent reversal of factor Xa inhibitors. *J Intensive Care*. 2018;6:34.
21. Schulman S, Gross PL, Ritchie B, Nahimiak S, Lin Y, Lieberman L, et al. Prothrombin complex concentrate for major bleeding on factor Xa inhibitors: a prospective cohort study. *Thromb Haemost*. 2018;118(5):842–51.
22. Kim BH, Lee S, Yoo B, Lee WY, Lim Y, Kim MC, et al. Risk factors associated with outcomes of hip fracture surgery in elderly patients. *Korean J Anaesthesiol*. 2015;68(6):561–7.
23. Kilci O, Un C, Sacan O, Gamli M, Baskan S, Baydar M, et al. Postoperative mortality after hip fracture surgery: a 3 years follow up. *PLoS One*. 2016;11(10):e0162097.
24. Douketis JD, Spyropoulos AC, Kaatz SO, Becker RC, Caprini JA, Garcia DA, et al. Perioperative bridging anticoagulation in patients with atrial fibrillation. *N Engl J Med*. 2015;373:823–33.
25. Douketis JD, Spyropoulos AC, Spencer FA, Mayr M, Jaffer AK, Eckman MH, et al. Perioperative management of antithrombotic therapy: antithrombotic therapy and prevention of thrombosis. 9th edition: American College of Chest physicians evidence-based clinical practice guidelines. *Chest*. 2012;141:e326S–50S.
26. Kearon C, Akl EA, Comerota AJ, Prandoni P, Bounameaux H, Goldhaber SZ, et al. Antithrombotic therapy for VTE disease: antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest*. 2012;141:e419S–94S.
27. Kaufman JA, Kinney TB, Streiff MB, Sing RF, Proctor MC, Becker D, et al. Guidelines for the use of retrievable and convertible vena cava filters: report from the Society of Interventional Radiology multidisciplinary consensus conference. *J Vasc Interv Radiol*. 2006;17:449–59.
28. Caplin DM, Nikolic B, Kalva SP, Ganguli S, Saad WE, Zuckerman DA, et al. Quality improvement guidelines for the performance of inferior vena cava filter placement for the prevention of pulmonary embolism. *J Vasc Interv Radiol*. 2011;22:1499–506.
29. Weinberg I, Abtahian F, Debiase R, et al. Effect of delayed inferior vena cava filter retrieval after early initiation of anticoagulation. *Am J Cardiol*. 2014;113:389–94.
30. Schulman S, Beyth RJ, Kearon C, Levine MN. Hemorrhagic complications of anticoagulant and thrombolytic treatment: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition). *Chest*. 2008;133(6 Suppl):257S–98S.
31. Patti G, Lucerna M, De Caterina R, et al. Thromboembolic risk, bleeding outcomes and effect of different antithrombotic strategies in very elderly patients with atrial fibrillation: a sub-analysis from the PREFER in AF. *Heart Assoc*. 2017;e005657. <https://doi.org/10.1161/JAHA.117.005657>

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