

Venous Thromboembolism and Postoperative Management of Anticoagulation

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KEYWORDS

• Deep venous thrombosis • Pulmonary embolism • Prevention

KEY POINTS

- The incidence of venous thromboembolism (VTE) after fracture repair has decreased over time, as a result of improved surgical technique and earlier mobilization.
- Hip fracture patients are considered to be in the highest risk category for VTE.
- All hip fracture patients should receive VTE prophylaxis, which may include pharmacologic and nonpharmacologic approaches.
- There are many pharmacologic options for VTE prophylaxis, and the choice should be based on each patient's characteristics and circumstances.
- Optimizing VTE prophylaxis requires consideration of both the risk of thromboembolism and bleeding risk.

INTRODUCTION/EPIDEMIOLOGY

The reported risk of venous thromboembolism (VTE) following hip fracture repair is substantial, but varies depending on how it was measured and when the study was completed. Earlier studies, which were placebo-controlled, showed that the incidence of VTE without prophylaxis ranged from 46% to 75%¹⁻⁴; however, many of these cases were determined through screening and were asymptomatic. The incidence of proximal deep venous thrombosis (DVT) is 27% without prophylaxis,⁵ and the rate of fatal pulmonary embolism (PE) has been estimated previously at 1.9%.⁶ VTE is the second most common complication following hip fracture surgery.⁷ Because of this, the American College of Chest Physicians (ACCP) puts hip fracture patients in the highest risk group.⁸

The incidence of VTE has decreased over time, as a result of improved surgical techniques, reductions in time to surgery, and earlier mobilization. Still, without

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prophylaxis, current estimates for symptomatic VTE are 4.3% within 35 days of surgery, with symptomatic DVT and PE incidence of 1.8% and 1%, respectively, in the first 10 to 14 days following surgery.⁹ With low molecular weight heparin (LMWH) treatment for 35 days, the incidence of symptomatic VTE is reduced to 1.8% (ie, a number needed to treat [NNT] of 40).

The rationale for thromboprophylaxis is multifold.⁸ As described previously, VTE following hip fracture surgery is common, and usually silent. Screening patients who are at risk is neither effective nor cost-effective. Morbidity (including symptomatic DVT and PE and postphlebotic syndrome) and mortality are high. Finally, thromboprophylaxis is effective at preventing symptomatic VTE and fatal PE, and has repeatedly been shown to be cost-effective.

The process of developing VTE starts early. In 1 study, 62% of those who waited 48 hours or more for surgery had venographic evidence of DVT.¹⁰ However, the presentation of symptoms is often delayed until after the initial hospitalization.¹¹ In 1 study, patients presented with DVT or PE a median of 24 days and 17 days after surgery, respectively.¹²

Hip fracture patients have many reasons for being at risk for VTE. Virchow triad requires the development of at least one of the following: venous stasis, vascular intimal injury, and hypercoagulable state.¹³ Following a hip fracture, patients can develop venous stasis due to immobility, as well as from supine positioning for surgery. Vascular intimal injury may occur at the time of the fracture or during surgery. A transient hypercoagulable state may occur from the release of tissue factors.

PATIENT EVALUATION OVERVIEW

The first step in evaluating patients for postoperative anticoagulation is to determine both their risk of VTE as well as their risk of bleeding. In addition to the risks common to all hip fracture patients, other factors increase risk further (**Box 1**). A history of malignancy increases risk of VTE, and metastatic disease confers higher risk than localized disease.¹⁴ Certain malignancies, such as pancreatic and stomach malignancies,

Box 1

Risk factors for VTE

Patient characteristics

- Age ≥ 85
- Malignancy
- Previous VTE
- Obesity
- Congestive heart failure
- Charlson comorbidity score ≥ 3
- Paralysis
- Presence of an inhibitor deficiency state

Surgical characteristics

- Surgical delay
- Prolonged surgery
- Extracapsular fracture

are associated with particularly high risk of VTE.¹⁵ A history of VTE, especially recent and/or unprovoked, increases risk. Presence of an inhibitor deficiency state, such as protein C, protein S, or antithrombin deficiency, increases the relative risk of VTE recurrence by up to threefold.¹⁶ The type of fracture may be important; in 1 large series, patients with extracapsular fractures (intertrochanteric or subtrochanteric) were twice as likely to develop symptomatic VTE as those with intracapsular fractures.¹⁷

The risk of bleeding is also important to consider. Different classification schemes have been developed to evaluate bleeding risk.^{18–21} The HAS-BLED scale²⁰ evaluates 1-year risk of major bleeding (defined as intracranial bleeding, bleeding requiring hospitalization, hemoglobin decrease >2 g/L, and/or transfusion) in patients with atrial fibrillation (Table 1). Most patients in the study cohort were taking oral anticoagulation medications, but the predictive capability was similar for those who were taking them and those who were not.

Condition	Points	Total	Bleeds Per 100 Patient-years
H Hypertension	1	0	1.13
A Abnormal liver or kidney function	1 or 2	1	1.02
S Stroke	1	2	1.88
B Bleeding tendency	1	3	3.74
L Labile international normalized ratio	1	4	8.70
E Elderly (>65)	1	5–9	Insufficient data
D Drugs or alcohol	1 or 2		

Hypertension is defined as systolic blood pressure >160 mm Hg. Abnormal kidney function is defined as the presence of chronic dialysis or renal transplantation or serum creatinine ≥ 200 $\mu\text{mol/L}$. Abnormal liver function is defined as chronic hepatic disease (eg, cirrhosis) or biochemical evidence of significant hepatic derangement (eg, bilirubin $>2\times$ the upper limit of normal, in association with aspartate transaminase/alanine transaminase/alkaline phosphatase $>3\times$ the upper limit of normal). Bleeding refers to previous bleeding history or predisposition to bleeding (eg, bleeding diathesis, anemia). Labile international normalized ratio refers to unstable/high international normalized ratios or poor time in therapeutic range (eg, <60%). Drugs/alcohol use refers to concomitant use of medications, such as antiplatelet agents and nonsteroidal anti-inflammatory drugs.

PHARMACOLOGIC TREATMENT OPTIONS

The ACCP recommends routine VTE prophylaxis in hip fracture patients.⁹ Several options are available, based on the patient's individual characteristics (Table 2). LMWH is recommended as the preferred agent (grade of evidence 2B), and should be started at least 12 hours before surgery, or 12 or more hours postoperatively (grade 1B). Aspirin was added to the list of options since 2008,⁵ and there was not consensus within the panel. Aspirin has been shown to be effective in reducing VTE risk in hip fracture, but less effective than LMWH.²²

Because many patients with hip fractures are already taking aspirin and/or clopidogrel for other comorbidities, the benefits of adding another anticoagulant medication need to be weighed against the additional risk of bleeding. A patient taking aspirin in addition to warfarin has almost twice the risk of bleeding, and a patient on both aspirin and clopidogrel in addition to warfarin has 4 times the risk.²³

The optimal duration of prophylaxis is unclear. One study comparing 1 week versus 4 weeks of anticoagulation following a hip fracture using fondaparinux showed

Table 2 ACCP 2012 recommendations for VTE pharmacologic prophylaxis	
Agent	Grade of Evidence
Low molecular weight heparin	1B
Fondaparinux	1B
Low-dose unfractionated heparin	1B
Warfarin	1B
Aspirin	1B

a reduction of VTE from 35.0% to 1.4%.²⁴ However, most of these cases were asymptomatic. The reduction in symptomatic VTE was more modest, at 2.7% versus 0.3%, for an NNT of 42. The rate of significant bleeding was 0.6% versus 2.4%, for a number needed to harm (NNH) of 56, although the rate of bleeding requiring reoperation was equivalent in the 2 groups. Because of the ongoing risk for symptomatic VTE after hospital discharge, the ACCP recommends extending thromboprophylaxis for up to 35 days after surgery.⁹

NONPHARMACOLOGIC TREATMENT OPTIONS

The most recent ACCP guidelines include intermittent pneumatic compression devices (IPCDs) as an alternative to pharmacologic prophylaxis (grade 1C).⁹ In patients with increased bleeding risk, either IPCDs or no prophylaxis is recommended. Patients who use IPCDs should wear the devices for 18 hours per day. Dual prophylaxis with pharmacologic treatment and an IPCD during hospitalization (grade 2C) is recommended for those who do not place a high value on the undesirable consequences of dual prophylaxis, such as discomfort and the potential for delirium. The NNT for symptomatic VTE is 63.⁹ Patients who receive LMWH will sustain 10 fewer symptomatic VTEs per 1000 patients (NNT 100) than those who are treated with IPCDs, at the expense of 10 additional major bleeds per 1000 patients (NNH 100).⁹

In patients who have contraindications to both pharmacologic and mechanical thromboprophylaxis, inferior vena cava (IVC) filter placement is sometimes considered. In a trauma population, the efficacy of PE prevention is high, with an NNT of 24.²⁵ However, this is balanced by the potential harms, including DVT at the insertion site, IVC occlusion, and filter migration. In a study of orthopedic patients with IVC filters placed for prophylaxis, 5% developed DVT.²⁶

Comprehensive VTE prophylaxis includes more than merely deciding what agent to use and how long to use it (**Box 2**). Other interventions, such as minimizing time to surgery, eliminating restraints, and early physical therapy, all help to reduce the time of immobility, thereby reducing venous stasis and limiting VTE risk. A systemic approach

Box 2 Comprehensive VTE prophylaxis includes
<ul style="list-style-type: none"> • Prompt surgery • Early weight bearing • Elimination of restraints • Delirium prevention • Pain management

that incorporates these elements, including pharmacologic and nonpharmacologic components, has been associated with low rates of VTE.²⁷

TO BRIDGE OR NOT TO BRIDGE

For patients who are admitted on warfarin and will be resuming warfarin after surgery, the question of whether to bridge with a short-acting anticoagulant arises. The goal of bridging is to minimize the time that a patient is not anticoagulated, but this must be balanced by early postsurgical bleeding risks.

The ACCP recommends resuming warfarin 12 to 24 hours after surgery, when hemostasis is achieved (grade 2C).²⁸ Patients can be divided into high (>10% annual risk of thromboembolism), intermediate (5%–10% annual risk) and low (<5%) risk patients. High-risk patients should receive bridging (grade 2C).²⁸ These patients include mechanical valve patients with mitral valve, caged-ball, tilting disc prosthesis or stroke or transient ischemic attack (TIA) within 6 months; atrial fibrillation patients with CHADS₂ (Congestive heart failure, hypertension, age >75, diabetes, stroke/TIA)¹⁸ score of 5 or 6, stroke or TIA within the past 3 months, or rheumatic heart disease; or VTE patients with VTE within the past 3 months or severe thrombophilia.

Data to support the approach to such patients are few; therefore, an individualized approach is required, based on a patient's specific comorbidities and risks, as well as the surgical procedure. For example, the ACCP lists joint arthroplasty as a procedure at high risk of bleeding during perioperative antithrombotic medication administration, so these risks must also be considered.

The use of bridging must also be considered within the context of the overall plan of care. If bridging would cause a significant delay to rehabilitation placement, the harms of a prolonged hospitalization could outweigh the incremental benefit of bridging a few more days.

SUMMARY

Fragility fracture patients are at high risk of postoperative VTE, both because of their injury and surgery, as well as their underlying frailty. Hip fracture patients are considered to be the highest risk group for VTE. Because of the high incidence and significant consequences of VTE, all patients should receive prophylaxis, which may include both pharmacologic and nonpharmacologic approaches. A comprehensive approach is multifaceted, and includes getting patients to surgery expeditiously and early mobilization. The decision of how to optimize prophylaxis is determined by evaluating the patient's risk of VTE and of bleeding, as well as his or her goals of care.

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