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Systematic Review

Venous Thrombosis Below the Knee: Prevention of Life and Limb Threatening Morbidity

Paul A. Stone, DPM, MBA, FACFAS*

Podiatrist, Castle Rock Foot & Ankle Care, Castle Rock, CO, USA.

***Corresponding Author:** Paul A. Stone, DPM, MBA, FACFAS, Podiatrist, Castle Rock Foot & Ankle Care, Castle Rock, CO, USA.*

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Abstract

The incidence of acute deep venous thrombosis is considered low compared with other orthopedic procedures such as knee and hip arthroplasty. The literature is still controversial with regards to chemical prophylaxis for treatment of foot and ankle trauma and surgery. It is crucial for the foot and ankle team to evaluate the potential risk factors for venous thrombosis with the goal of preventing the complications of post-phlebitic syndrome, pulmonary hypertension, and fatal pulmonary embolus. This article reviews the current literature, risk stratification scoring methods, and makes recommendations for chemical prophylaxis for high risk patient populations.

Keywords: *Thromboprophylaxis, Deep venous thrombosis, Risk stratification, Pulmonary embolism, Risk assessment tools, Blood clot, Acute Arterial thrombosis, Atherosclerosis.*

Introduction

Deep venous thrombosis and pulmonary embolus, although infrequent, remain two of the most morbid conditions for podiatrists to consider when treating both surgical and non-surgical conditions. In the United States it is the number 1 cause of unexpected deaths. (32) The reported incidence of calf deep venous thrombosis ranges from 0.05-3.5%. Pulmonary embolus incidence is much lower at 0.037-.34% with mortality from pulmonary embolus exceedingly low. However, propagation of calf thrombosis causing fatal pulmonary embolization still exists and remains a significant concern in high-risk podiatric patients. This review discusses those risks and helps decision makers consider when to use chemical prophylaxis when treating both surgical and non-surgical conditions. This article discusses specific risk factors for developing calf thrombosis and the risk assessment tools currently available to stratify those specific patients for chemoprophylaxis. A one-size-fits-all approach to preventing deep venous thrombosis for podiatry patients currently does not exist. Ultimately, the decision to prescribe chemical prophylaxis during nonoperative or operative management of foot and ankle disorders should be based on each patient's unique risk-benefit analysis (5).

Incidence of Calf Thromboembolism

Mizel, et al, evaluated 2733 patients for preoperative risk factors and postoperative thromboembolic events (1). The use of postoperative VTE prophylaxis, if any, was determined by the surgeon, and medication, dose, duration, and other pertinent information was not provided in the article. The incidence of DVT was 0.22%, and that of nonfatal PE, 0.15%. No patient experienced a fatal PE. The authors reported that the frequency of fatal PE after foot and ankle surgery appears to be less than 0.037%. Based on these results, the authors concluded that routine prophylaxis for thromboembolic events after foot and ankle surgery is probably not warranted. They also found that the only statistically significant relationships with thromboembolic events were postoperative regimens of non-weightbearing and cast immobilization. All patients with thrombotic events had been treated postoperatively with immobilization and non-weightbearing, with a thromboembolism incidence of 6 of 1150 (0.22%).

The incidence of DVT after foot and ankle surgery was also studied by Solis and Saxby (2). The study involved 201 patients, none of whom received DVT prophylaxis, and underwent bilateral calf duplex ultrasound at their first postoperative visit. Deep calf clots were found in 3.5%, but none showed progression on follow-up ultrasound or extension proximal to the calf. None of these patients had any clinical symptoms. These authors also concluded that the rate and progression of DVT after foot and ankle surgery is low and does not require routine prophylaxis, even in high-risk patients. They also noted that postoperative immobilization (p=0.053), hindfoot surgery (p=0.02), increased tourniquet time (p=0.03), and advancing age (p=0.051) were associated with risk of DVT formation. The article did not specify what constitutes increased tourniquet time or advancing age. Based on this study findings and review of the literature, Solis and Saxby agree with Mizel et al. that routine DVT prophylaxis is not indicated in patients undergoing foot and ankle surgery.

Deep venous thrombosis can occur as early as one week after surgery or trauma, although the onset typically is around three to four weeks. (34)

The incidence of pulmonary embolism was reported in 2016 by Alvin Wu, et al. (3). The risk among patients with deep venous thrombosis below the popliteal is unclear, and evidence regarding how to manage these patients is insufficient. The lack of robust evidence regarding the role of anticoagulation for calf DVT creates a void of guidance for clinical decision making. This systematic review states that all previous studies failed to demonstrate the significance of anticoagulation therapy for preventing calf DVT propagation. Early results from the CACTUS-PTS trial suggest that anticoagulation has no significant effect on composite outcomes, let alone PE. Calf DVT patients with concurrent PE may have had a proximal DVT that embolized and because this cannot be determined, allocating calf DVT the cause is not appropriate. Autopsy studies can only demonstrate the presence of an isolated calf DVT in patients who are thought to have died of PE but cannot link the two findings directly.

Soohoo studied 57,183 patients who underwent ORIF of an ankle fracture in the California database during an 11-year period (4). The overall rate of DVT within 90 days of surgery was 0.05%. The rate of pulmonary embolism was 0.34%. The article, published in 2011, indicated that up to 80% of providers in the US do not employ routine thromboprophylaxis following foot and ankle surgery. In addition to the low reported rates of VTE in foot and ankle surgery, studies investigating various anticoagulants have not shown remarkable decreases in DVT and PE rates.

Claveau studied 425 patients between June 2017 to December 2018 who underwent both elective and trauma surgery of the foot and ankle (26). Each patient received 81 mg aspirin, 325 mg aspirin, or 2.5 mg Apixaban BID post-operatively. The incidence of DVT and PE was 1.2% and 0.2% respectively. The authors recommended routine prophylaxis to prevent VTE in patients who require immobilization and are over 60 years old. Patients with multiple comorbidities such as obesity, history of smoking, peripheral vascular disease, previous history of DVT, and extended tourniquet use should be taken into consideration.

Weighing the Risk Factors for DVT and PE

While there are multiple risk factors for developing thromboembolism, some risk factors are considered primary and others secondary. Risk factors tend to be cumulative, making patients with multiple comorbidities a higher risk for clots. The literature is not consistent in weighing the secondary risk factors. However, the primary risk factors are consistent.

The primary risk factors for thromboembolism include:

1. Prior DVT
2. Hypercoagulability
3. Cancer
4. Immobilization >4 weeks

Secondary risk factors vary throughout the literature with some articles highlighting some which others downplay:

Age >60

BMI >30

Family history of DVT Oral Contraceptive use Varicose veins

Non-weightbearing, Achilles rupture, Ankle fracture, Total ankle replacement, Major arthrodesis, Severe foot injury.

Bed rest

Pregnancy

Inflammatory Bowel Disease

Peripheral vascular disease

Airline flight >6hrs.

Age

According to literature outlined in the ACFAS consensus statement (5), the risk of DVT increases with advancing age, being more common over the age of 50 and increasing thereafter. In the article "Venous Thrombosis After Hallux Valgus Surgery," consecutive patients undergoing chevron bunionectomy for correction of hallux valgus deformity were enrolled in the study. Patients with clinical or hematological risk factors for venous thrombosis were excluded. One hundred patients with a mean age of 48.9 years were operated on and did not receive medical prophylaxis against thrombosis. All patients were assessed with phlebography at a mean of twenty-nine days postoperatively.

Venous thrombosis was found in four patients (4%). The mean age of these patients (and standard deviation) was 61.7 ± 6.1 years compared with a mean age of 48.4 ±13.9 years for the patients in whom thrombosis did not develop ($p = 0.034$). (23)

Soohoo studied 57,183 patients who underwent ORIF of an ankle fracture in the California database during an 11-year period (4). Rates of pulmonary embolism were elevated in patients over 75 years of age.

Age has been determined to increase the risk of venous thromboembolism by 2% per increase in year (24).

Use of Tourniquet

Use of tourniquet. According to literature outlined in the ACFAS consensus statement, "It is unclear whether tourniquet use including dependence on location or duration pose any significant excess risk for DVT."

Immobilization

CAM (controlled ankle motion) and non-weightbearing are identified as important secondary risk factor for DVT. Mizel, et al. found that the only statistically significant relationships with thromboembolic events were postoperative regimens of non-weightbearing and cast immobilization (1).

Obesity

Increased BMI, according to the ACFAS consensus statement, is an independent secondary risk factor for DVT. "The variability and lack of association reported in some foot/ankle studies make it difficult to quantify the magnitude of its effect." Obesity, generally defined as a BMI over 30, is cited as a secondary risk factor in numerous studies.

Hypercoagulability

Hypercoagulability remains the great unknown variable in determining DVT risk. There is no simple pre-operative screening test for even the most common types of hypercoagulability thrombophilia syndromes, including, but not limited to: Factor V Leiden, antithrombin III deficiency, protein C and protein S deficiency, hyperhomocysteinemia, acquired anti-phospholipid syndrome, (lupus anticoagulant). Patients with heterozygous Factor V Leiden are 7x more likely to develop thrombosis. Patients with homozygous factor V Leiden are 80x more susceptible (11).

Testing for hypercoagulability remains a controversial topic. Gupta retrospectively reviewed electronic medical records for patients undergoing inpatient thrombophelia testing at a community hospital during 2018 (28). The authors found that most inpatients were tested while in acute thrombosis or on anticoagulation therapy which was deemed inappropriate.

The hypercoagulable panel consist of the following tests:

1. Protein C level
2. Protein S level
3. Antithrombin III
4. Factor V Leiden
5. Prothrombin gene mutation
6. Anti-Beta2 glycoprotein
7. Anticardiolipin antibodies
8. Lupus anticoagulant

Each of these components on the panel can be tested individually, typically by PCR testing. The tests may be also ordered as a hypercoagulation panel, which costs between $1,370-$2,986.

The decision to order a hypercoagulation panel or an individual test pre-operatively should be based on the patient's personal and family history. The mutation resulting in Factor V Leiden is present in 2-7% of the Caucasian population. A whole blood screening test for Factor V Leiden using a Russell Viper Venom time-based assay is presently available in a point-of-care setting. (29)

Smoking

There is insufficient evidence supporting the role of smoking as a risk factor for DVT. Studies in surgical patients suggest that smoking has either no effect or a protective effect on the development of post-operative DVT. (35) Smoking is suggested to be a risk factor primarily in morbidly obese patients.

Past History of Thromboembolism

According to Edmonds, et al., a past history is the single most important risk factors for subsequent DVT (11). Patients with a history of DVT have a 25% recurrence rate over the subsequent 10 years (12).

Hormone replacement and oral contraceptives

Estrogen has prothrombotic effects increasing risk of VTE by increasing prothrombin and decreasing antithrombin III. Estrogen increases the levels of factors VII and X, as well as decrease the levels of anticoagulant proteins. Third generation progestins have a 2-fold higher risk of VTE compared to second generation, especially within the first 6 months of use (13). Postmenopausal estrogen replacement is associated with an increased risk for venous thromboembolism, and this risk may be highest in the first year of use (14).

Cancer

Cancer causes hypercoagulability through increased production of procoagulant factors and cytokines as well as through the interaction of malignant cells with the inner lining of the blood vessels.

Autoimmune Disorders including Inflammatory Bowel Disease and Antiphospholipid Syndrome

Antiphospholipid syndrome is an autoimmune disorder caused by the presence of auto-antibodies directed to phospholipids, which are components of the cell membrane. The most frequently found antibodies are lupus anticoagulant, anticardiolipin, and anti-beta-2-glycoprotein. Individuals with antiphospholipid syndrome have a high risk of developing arterial and venous thrombosis, as well as obstetric complications like miscarriage.

Achilles Rupture and Repair

Injury and repair of the Achilles tendon has been implicated as a risk factor for the development of calf deep venous thrombosis. Studies have published conflicting results. In a Swedish study of 251 patients with acute Achilles tendon rupture were retrospectively analyzed. Symptomatic and asymptomatic DVT incidence at 2 and 6 weeks post repair was assessed using compression duplex ultrasound. The total DVT incidence was 49%. Propagation of the thrombus occurred in 7% of the patients with calf DVT. There were no symptomatic pulmonary embolisms reported during the follow-up period.

Bullock studied 113 patients following non-elective and elective Achilles tendon repair. Their incidence of DVT was 2.65% and of PE 1.7%. All of the deep venous thromboembolism cases occurred in chronic Achilles repair patients.

Blanco found that patients with Achilles rupture had a slightly higher risk of DVT when compared to ankle fracture patients 3.88 vs 2.51%. (33) The authors also found that the DVT develops quicker in the Achilles rupture patients compared to the ankle fracture group (16 vs. 37.2 days)

Peripheral Vascular disease

Virchow's Triad consist of hypercoagulability, stasis of blood flow, and endothelial injury. Vascular endothelial damage from long-term atherosclerosis can increase the risk of arterial and venous thromboembolic events.

Soohoo studied 57,183 patients who underwent ORIF of an ankle fracture in the California database during an 11-year period (4). The highest rates of DVT were seen in patients with peripheral vascular disease at 0.34% and the rates of PE were elevated in patients with peripheral vascular disease at 1.03%.

One of the most important recent findings is that atherosclerosis may develop differently depending on the anatomic level of the leg. In studies of patients who underwent amputation, histologic evaluation of arteries from above-knee amputations (AKA) compared to below-knee amputations (BKA) show marked differences.35 AKA arteries have a similar appearance to those of diseased coronary arteries and show greater medial calcification and acute thrombi, which are typical atherosclerotic changes within coronary plaque, while BKA arteries had a greater number of chronic thrombi (an atherothrombotic process) and less typical plaque signs.33 Although thrombin is a major factor in the development of PAD, antiplatelet therapy, the most common pharmacologic therapy utilized for PAD, does not have a significant effect on thrombin. The most effective inhibitor of thrombin are anticoagulant agents, but bleeding risk is of concern. Recently the Factor 10a inhibitor drug rivaroxaban, in a low "vascular dose" (2.5 mg) given twice daily along with low-dose (81 mg) aspirin given once daily has shown to be superior to aspirin alone in the treatment of PAD.36,37 This "dual pathway" combination has been approved by the US Food and Drug Administration (FDA) for the treatment of stable PAD and following recent lower-extremity revascularization (LER) due to symptomatic PAD. (38,39)

Acute Arterial thrombosis risk and prevention

Atherosclerosis is a known risk factor for arterial thrombosis. Most arterial thrombotic events have a clear atherosclerotic or cardioembolic etiology. Nonatherosclerotic and noncardioembolic arterial events are referred to as unexplained arterial thrombosis.

Acute arterial thrombosis can have a devastating effect when showers of emboli occlude the major distal extremity arteries. We presented a case in 1994 of an otherwise healthy young adult who developed acute limb ischemia due to a nonatherosclerotic and noncardioembolic arterial event which resulted in a below-knee amputation. (30) Etiology of the arterial thromboembolism was never discovered. There is an assorted list of factors that can precipitate an arterial event including primary hypercoagulable disorders, but also pro-thrombotic medications or substances, vascular and anatomic abnormalities, and undiagnosed systemic disorders, such as malignancy and autoimmune diseases. The role of thrombophilia's in arterial thrombosis is not well-defined, as opposed to venous thrombosis in which thrombophilia's have been more extensively studied. The antiphospholipid syndrome (APS), however, has a well-documented increased venous and arterial thrombotic risk.

Why not just use Aspirin?

Aspirin would appear to be the ideal tool to use to help prevent thromboembolism. It is inexpensive, readily available, over-the-counter, requires no monitoring, has few side effects in gastro-intact patients, and has few drug interactions. Unfortunately, aspirin is not the panacea for DVT prevention. In fact, aspirin is generally only recommended for thromboembolism prophylaxis in ambulatory patients following knee and hip arthroplasty. Relying on aspirin for chemical prophylaxis may provide a false sense of comfort without substantial benefit.

According to the 2015 American College of Foot and Ankle Surgeons' clinical Consensus Statement (5), "Risk, Prevention, and Diagnosis of Venous Thromboembolism Disease in Foot and Ankle Surgery and Injuries Requiring Immobilization," there is insufficient evidence to support the use of aspirin as an isolated measure of prophylaxis in high-risk patients (5).

A 2017, JBJS reports Acetylsalicylic acid (aspirin) is an agent for VTE prophylaxis following arthroplasty. Many studies have shown its efficacy in minimizing VTE under these circumstances. It is inexpensive and well-tolerated, and its use does not require routine blood tests (6).

In a 2012 seminal article on aspirin and thromboembolism, Griffiths evaluated 2654 patients undergoing elective foot and ankle surgery from 2003-2010.

1078 received 75 mg ASA and 1576 received no chemical prophylaxis.

Griffiths found that 75mg ASA has no protective effect. The incidence of DVT was 0.42%. The incidence of PE was 0.15% (7).

A 2019 study found no difference in the use of 81mg Aspirin BID vs. 325mg Aspirin BID for patients undergoing THA between 2012 and 2016. The 90-day incidence of symptomatic VTE was 1.0% in the 325-mg group and 0.6% in the 81-mg group ($p = 0.35$). Symptomatic DVT incidence was 0.8% in the 325-mg group and 0.5% in the 81- mg group ($p = 0.49$). The incidence of symptomatic PE was 0.3% in the 325-mg group and 0.2% in the 81-mg group ($p = 0.45$). Furthermore, bleeding was observed in 0.8% of the 325-mg group and 0.5% of the 81-mg group (8).

In 2008, The American Academy of Chest Physicians recommends against ASA for DVT prophylaxis. In 2012 The American College of Chest Physicians accepts ASA for TKA and THA procedures. The most recent update discussing aspirin's role in 2016 AACP cautions use of ASA alone (9).

National Institute for Health and Care excellence (NICE) guidelines do not regard aspirin as adequate prophylaxis for DVT (10).

What are the Current Accepted Scoring Methods to determine Level of Risk for Thromboembolism?

The Wells criteria for calculating the risk of deep venous thrombosis and pulmonary embolus are commonly used in the emergency department to stratify emergent patients for further diagnostic evaluation and treatment of venous thromboembolic conditions. (22)

The Wells Criteria for calculating risk of DVT assigns 1 point for each of the following symptoms:

a. Cancer

b. Bedridden for > 3 days

c. Calf swelling > 3cm compared to other leg

d. Entire leg swollen

e. Localized tenderness +Homans or Pratt's test

f. Pitting edema

g. Previous DVT

h. Collateral superficial veins non-varicose present

i. Paralysis, paresis, or recent plaster immobilization of lower extremity

j. Alternative diagnosis of DVT as likely or more likely -2 points.

Interpreting the Wells Criteria for DVT.

<2 low risk, DVT unlikely

The Wells Criteria for calculating risk of PE assigns points for each of the following symptoms:

a. Clinical signs and symptoms of DVT (3 points)PE is #1 diagnosis or equally likely. (3 points)
b. Tachycardia >100. (1.5 points)
c. Immobilization at least 3 days or surgery in the previous 4 weeks. (1.5 points)
d. Previously diagnosed PE or DVT. (1.5 points)
e. Hemoptysis. (1 point)
f. Malignancy with treatment within 6 months or palliative. (1 point)

Interpreting the Wells Criteria for PE Scores <4 are low risk, PE unlikely.

Pulmonary embolism after ankle surgery is a remarkably rare event. Death from PE after ankle surgery is rare with a frequency of less than 0.037% (17).

Mizel found the risk of VTE after foot and ankle surgery is 0.22%; the risk of PE after foot and ankle surgery is 0.15% (1).

Shibuya et al. examined 75,664 patients in National Trauma Data Bank (a database focused on higher energy trauma patients) undergoing foot and ankle fracture surgery and found the incidence of DVT to be 0.28% and the incidence of PE risk to be 0.21% (15).

Venous Thromboembolism (VTE) Risk Assessment Tools

In 2008, the Surgeon General announced a "call to action" to prevent deep vein thrombosis and pulmonary embolism in the hospital setting. In 2009, CMS issued the final rule in the Inpatient Prospective Payment System which considered ten conditions for prospective payment. This included Deep Vein Thrombosis (DVT)/Pulmonary Embolism (PE) following Certain Orthopedic Procedures defined as total knee and hip arthroplasty. Thereafter, hospitals and surgery centers developed a Venous Thromboembolism (VTE) Risk Assessment Tool which is typically completed by the pre-operative nursing staff at the surgical facility and signed off by the attending surgeon prior to the surgical start time. The risk factors pertinent to lower extremity surgeries include:

Age

Swollen legs Obesity Smoking

Oral contraceptives

Immobilization more than three days pre-op Anticipated surgery time in the operating room Use of tourniquet, location not specified Immobilization in a cast within last 30 days Cancer

Prior DVT

History of blood dyscrasia or bleeding disorder

The risk assessment tool varies between facilities. Surgeons should be familiar with the various forms of this tool at the facilities in which they perform their admissions and surgical cases. A sample of a typical surgery center Venous Thromboembolism (VTE) Risk Assessment Tool is attached in appendix A.

In addition to the Venous Thromboembolism (VTE) Risk Assessment Tool, the two currently validated risk assessment models are the L-TRiP (cast) and the Caprini Risk Assessment tool.

Leiden-TRiP Prediction with Cast Score. 2015.

Leiden-TRiP Prediction with Cast Score helps predict risk of DVT using the parameters of trauma, immobilization, other factors. Each risk factor is assigned a numerical score. The cumulative sum of the total score is then used to stratify patient risk and the recommendation for chemoprophylaxis.

Appendix A

Venous Thromboembolism (VTE)
Risk Assessment
Procedure:

Ht: Wt: BMI:

EXCLUSION FACTORS

Age: Weight:

- ☐ Local anesthesia planned
- ☐ Monitored anesthesia care planned
- ☐ Patients less than 16 years of age
- ☐ Surgery/procedure time 45 minutes or less

NO FURTHER ASSESSMENT REQUIRED ON EXCLUDED PATIENTS

STEP 1: IDENTIFY CLINICAL RISK FACTORS (GIVE EACH ITEM IDENTIFIED THE APPROPRIATE SCORE)

EACH RISK FACTOR REPRESENTS (1) POINT	EACH RISK FACTOR REPRESENTS (2) POINTS
Patient is 41-60 years old	Patient is 61-74 years old
History of general surgery lasting more than 45 min in past 30 days	Malignancy-except skin (present or previous history)
Varicose Veins	Scheduled major surgery 61 min or greater
Inflammatory Bowel Disease	Lower extremity immobilizing cast within last 30 days
Swollen legs (present on admission)	Central venous access less than 31 days preop
Obesity (BMI > 30)	**EACH RISK FACTOR REPRESENTS (3) POINTS**
Smoking/Chewing Tobacco use	Hx of DVT/PE (any time)
Birth Control or Hormone replacement therapy	Patient is 75 yrs old or greater
☐ COPD / ☐ CHF / ☐ Pneumonia / ☐ AFIB	History of any type blood dyscrasia or bleeding disorder
Pregnancy or less than 30 days Post Partum	Scheduled major surgery with additional medical risk factors: ☐ MI, ☐ CHF, ☐ Sepsis, or ☐ serious lung disease
Immobilization > 3 days pre-op	**EACH RISK FACTOR REPRESENTS (5) POINTS**
Use of beach chair positioner during surgery	Total joint replacement or hip, pelvis or leg fracture within the last 30 days
Use of tourniquet during surgery	History of stroke and/or TIA
Scheduled surgery time 46 to 60 minutes	

☐ **TOTAL SCORE THIS COLUMN (1)** ☐ **TOTAL SCORE THIS COLUMN (2)**

STEP 2: TOTAL RISK FACTOR POINTS

Total Risk Factor Points (Total of column 1 and 2): ☐

STEP 3: DETERMINE PROPHYLAXIS

Order required.

TOTAL POINTS	RISK LEVEL	SELECT APPROPRIATE PROPHYLAXIS REGIMEN BASED ON TOTAL RISK POINTS
0-1	Low	☐ No specific measures; OR ☐ Educate on early ambulation
2	Moderate	☐ SCD ☐ Early ambulation
3-4	High	☐ SCD ☐ Early ambulation
5 or more	Highest	☐ SCD ☐ Early ambulation

*Contraindications for SCD therapy may include HX of severe peripheral arterial disease, current HX of CHF, existing DVT

I have reviewed the above risk factors and have ordered the appropriate prophylaxis.

Physician Signature **Nurse Signature**

Trauma:

High-risk trauma 3

examples: Pilon fracture, Achilles tendon rupture,

Intermediate-risk trauma 2

examples: Bi or tri-malleolar ankle fracture, Ankle dislocation, Lisfranc injury, Severe ankle sprain

Low-risk trauma 1

examples: Single malleolar ankle fracture, Metatarsal bone(s) or forefoot fracture, Significant muscle injury

Immobilization:

Upper-leg cast 3

Lower-leg cast or CAM Walker boot 2 Foot cast 1

Surgical shoe 0

Age:

Age <35 years 0

Age 35 and <55 years 1

Age 55 and <75 years 2

Age 75 years 3

BMI:

Body Mass Index BMI 25 and <35 kg/m 2

1 Body Mass Index BMI 35 kg/m2 2

Other:

Family history of VTE (first-degree relative) 2

Personal history of VTE 4

Current use of oral contraceptives / Estrogenic hormone therapy 4

Cancer diagnosis within the past 5 years 3

Chronic venous insufficiency (varicose veins) 1

Interpretation of the Leiden-TRiP Prediction with Cast Score:

Score<7 no anti-coagulation

Score≥7 consider anti-coagulation

Caprini Score

The Caprini Score is another published criteria which helps predict the risk of DVT. The Caprini Score was developed for hospitalized patients. This scoring system has not been tested in the outpatient setting (21).

Each risk factor = 1 point

Oral contraceptives or hormone replacement therapy (I removed a lot of punctuation below)

Age 41-60 years
Minor surgery
Varicose veins Obesity,

BMI >30
Swollen leg
Each risk factor = 2 points

Age 60-74 years
Surgery (>60 minutes)
Previous malignancy
Morbid obesity (BMI >40)

Each risk factor= 3 points

Age over 75 years

Major surgery lasting 2-3 hours

BMI >50

History of DVT/PE
Family history of DVT/PE
Present cancer or chemotherapy
Positive Factor V Leiden;
Positive Prothrombin
Elevated serum homocysteine
Positive Lupus anticoagulant
History of Heparin-induced thrombocytopenia (HIT)

Caprini Score interpretation:

The American College of Chest Physicians, ninth edition 2012, defines the high-risk group as a score of 5 or greater for general surgery patients. Krauss, et al. found that total joint arthroplasty patients (THA) and (TKA) with a score of 10 or greater were at high risk of VTE. There are no recommendations for patients undergoing podiatric surgery in the Caprini model.

Caprini Score interpretation

Recommended duration of chemoprophylaxis

1-2	low risk	During hospitalization
3-4	moderate risk	During hospitalization
5-8	high risk	7-10days total
>9	highest risk	30 days total

Patient Reported Symptoms of DVT and PE

In healthcare, a differential diagnosis is a method of analysis of a patient's history and physical examination to arrive at the correct diagnosis. It involves distinguishing a particular disease or condition from others that present with similar clinical features.

Deep vein thrombosis (DVT) symptoms should be included in the differential diagnosis in patients who present with:

- Acute Leg swelling
- Leg pain, cramping or soreness that often starts in the calf
- Change in skin color on the leg
- A feeling of warmth on the affected leg

Deep vein thrombosis can often present as a silent condition without noticeable symptoms.

Symptoms of a pulmonary embolism include:

- Dyspnea
- Chest pain
- Vertigo or lightheadedness
- Syncope
- Tachycardia
- Tachypnea
- Hemoptysis

What is the Appropriate Testing Regimen for Calf DVT

Duplex ultrasound remains the current standard diagnostic test to screen for DVT. Venography was replaced in the 1980s by ultrasound due to its use of intravenous dye which carries the risk of anaphylaxis and renal impairment. Duplex ultrasound is technician sensitive and studies have shown the modality to have better sensitivity in the thigh veins than the calf. A systematic review and meta-analysis of the diagnostic accuracy of ultrasonography for deep venous thrombosis by Goodacre, S. et al. concluded that the sensitivity of distal ultrasound for detecting thrombosis in the calf veins was 64.6 to 77.2% compared to 96% in the proximal thigh veins (20).

D-Dimer

D-Dimer is a marker of endogenous fibrinolysis. This screening test has a high negative predictive value making it a valuable test in the emergency department for patients with symptoms suggestive of VTE. Its value in podiatry is limited as duplex ultrasound remains the current standard diagnostic tool. D-Dimer can be considered when ultrasound or venography may not be available, such as in patients for example who are post Achilles rupture or repair, compound tibial fracture, and post-op gastrocnemius recession. D-Dimer may be helpful as a screening tool as the muscular veins may not be easily visualized with ultrasound.

What is the Appropriate Chemical Prophylaxis?

In addition to mechanical prophylaxis which typically consists of compression stockings on the contralateral leg and intermittent compression during surgery, chemical prophylaxis is recommended for patients with increased risk of thrombosis. Medications for DVT prevention include:

Low Molecular weight heparin Ultra-fractionated heparin Coumadin (warfarin)

Eliquis (apixaban) 2.5 mg b.i.d. Xarelto (rivaroxaban) 10 mg q.d.

Pradaxa (dabigatran) 150-220 mg q.d. (Factor IIa thrombin inhibitor)

Abelacimab is a new Factor XI inhibitor which acts by inhibiting the activity of factor XI. Abelacimab is a monoclonal antibody that prevents activation of Factor XI or thrombin (Factor IIa)

Factor XI has appeared most promising due to its lower risk of bleeding risk. It has a long half life of 30 days allowing monthly administration. The medication is still in phase 3 trials at this time.

Factor XII inhibitors under investigation currently. Also intrinsic coagulation pathway inhibitor , like Factor XI inhibitor Abelacimab, it also has a lower bleeding risk and better safety profile than the vitamin K inhibitors and heparin analogs.

In 2017, the Medical Associations in Germany developed guidelines on the prevention of venous thrombosis. The risk is considered to be increased if at least one of the following risk factors is present:

Previous venous thrombosis
Blood clotting disorder
Cancer
>60 years old
BMI >30

Patients without any of these risk factors were encouraged to move their legs again as soon as possible which they felt was enough in their case (16).

In a recent worldwide survey, Zambelli sent an online questionnaire to 693 orthopedic surgeons from six continents, Europe 129 surgeons, North America 292, Latin America 174, Oceana 37, and Africa 27. (25)

Most orthopedic surgeons responded that thromboprophylaxis was sometimes needed but the type of anticoagulant varied in different continents. Aspirin was the prophylactic agent of choice in the United States. In a previous publication from 2021, Zambelli reported that current studies lack evidence for a universal thromboprophylaxis recommendation in ankle and foot surgeries. (31) Once chemical prophylaxis is indicated by risk factor stratification, Low molecular weight heparin was deemed the agent of choice.

The authors concluded that more than half of the orthopedic surgeons surveyed reported that no hospital or national guidelines for VTE prophylaxis in foot and ankle surgery existed in their institution. This indicates that the existing guidelines are not well known among orthopedic surgeons across the world. (25)

Conclusion

Despite the data for foot and ankle surgery associated thromboembolic complications, there are no clear recommendations for prophylaxis of VTE. The decision and methods of prophylaxis can be considered only in the high-risk patient. Moreover, the agent of choice used for anticoagulation is not clear and should be individualized. Routine VTE prophylaxis is not recommended after foot and ankle surgery; those with multiple risk factors should be considered for VTE prophylaxis.

In addition to mechanical prophylaxis with compression stockings on the contralateral leg and intermittent compression during surgery, chemical prophylaxis for the prevention of venous thromboembolism can be helpful. However, even with the use of appropriate dose anticoagulant prophylaxis, deep venous thrombosis may still occur. Cochrane researchers found that 25 out of 1,000 people who are immobilized in a cast or brace who did not receive LMWH developed DVT with noticeable symptoms (2.5%) compared to 3 out of 1,000 who received low molecular weight heparin injections (0.3%).

Although the current VTE Risk Assessment Tools can be used to help stratify higher risk patients who may benefit from chemical prophylaxis, however, the chemical prophylaxis agent, dose, and duration have not been clearly defined. It is currently not appropriate to give every patient undergoing treatment for a foot or ankle injury or undergoing surgery chemical prophylaxis due to the low risk of VTE, high cost of the medication, and the risk of bleeding.

At the completion of this review of current studies on the risk and prevention of thromboembolism the author recommends that the following patients be given high consideration for venous thromboprophylaxis in of both surgical and non-surgical patients treated for foot and ankle conditions:

Risk factors are cumulative:

1. Prior DVT
2. Hypercoagulability syndromes including inherited and acquired conditions
3. Cancer, active or treatment within the past 6 months
4. Prolonged non-weightbearing immobilization in a cast or boot

The following patients should be given moderate consideration for venous thromboembolism prophylaxis in the treatment of both surgical and non-surgical patients treated for foot and ankle conditions. It is prudent to remember that risk factors for VTE are cumulative:

1. Age >60
2. BMI >30
3. Positive family history of DVT
4. Oral Contraceptive or hormone replacement use
5. Achilles tendon repair

Additional risk factors discussed in this review should be given consideration to prescribe prophylaxis during nonoperative or operative management of foot and ankle disorders should be based on each patient's unique risk-benefit analysis taking into account that the risk factors are cumulative.

Limitations

This systematic review attempts to cumulate the current available literature and make recommendations for prophylaxis of venous thrombosis in foot and ankle trauma and surgical treatment. There are numerous risk factors of which several are highlighted. Other risk factors, such as prior MI, renal dialysis, atherosclerosis, cocaine and anabolic steroid use, have also been associated with a higher risk of venous thromboembolism as secondary risk factors. While all reasonable risk factors should be considered, the literature lacks sufficient evidence to recommend or not recommend chemical prophylaxis for each risk. The literature is also debatable regarding the type of anticoagulant or antiplatelet drug or a combination therapy to recommend. The world literature is vague with regards to the timing and duration of anticoagulation and the arguable option to discontinue anticoagulation once the patient is ambulatory or switch to aspirin therapy at some point in the therapy. Therefore, recommendations on these topics cannot be made at this time.

Conflict of Interest

The author declare no conflict of interest.

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