INTRODUCTION
Venous thromboembolism (VTE) consisting of both deep venous thrombosis (DVT) and pulmonary embolism (PE) rates are 1 to 2 per 1,000 person-years and increases with age to 1% per year (1). The lifetime risk for VTE is approximately 11% (1-3). VTE results in more than 100,000 deaths in the US each year. This is greater than breast cancer and motor vehicle accident deaths combined (4-6). VTE is the third leading cause of death in hospitalized trauma patients with an estimated incidence of 5-20% even with prophylaxis (7-9). In 2008, the Surgeon General Steven K. Galson published a “Call to Action” on VTE prevention (5). Galson proposed that VTE was a major health risk and encouraged evidence-based research to reduce and prevent VTE and its sequelae.

Relative to foot and ankle surgery, there are limited data and there are widely varying levels of VTE risks for this subset of patients. Jameson et al in a large series of patients found similar rates of 0.3% for each type of surgery including total ankle replacement, hindfoot fusion, ankle fracture repair, and first metatarsal surgery (10). Another study by Mizel et al of 2,733 patients followed for 90 days found DVT rates of 0.22% and PE of 0.15% (11). Both of these studies would not indicate that prophylaxis was warranted. However, other studies reported much higher rates of VTE. Lapidus et al suggested DVT rates of 28% for ankle fracture repair (12) and 36% for Achilles tendon rupture (13). Solis and Saxby found foot surgery DVT rates of 3.5% (14). These higher levels of DVT risk would suggest that prophylaxis is warranted. Relative to foot and ankle disorders, application of a lower extremity cast increases risk of DVT by 8 times in one study (15). However a large meta-analysis reported rates of VTE between 0-5.5% (16) in the cast immobilized population. Therefore cast immobilization alone is not likely to warrant prophylaxis.

WHEN TO GIVE PROPHYLAXIS
CHEST has long been publishing recommendations on prevention and treatment of VTE. In one article, they do not recommend prophylaxis for patients with isolated lower leg injuries requiring leg immobilization (17). However, no effort is made to stratify the risk as all patients immobilized for 1 week were included and no other criteria stratified. This was graded as a 2C recommendation (on a scale where 1 = a strong recommendation, and 2 = a weak recommendation). The C refers to weak evidence where B is moderate and A is high-quality evidence.

ACFAS RECOMMENDATIONS
In 2015, the American College of Foot and Ankle Surgeons published a clinical consensus statement outlining their recommendations for prophylaxis and treatment of VTE (18). Their aim was to answer 4 questions with the best available evidence-based data. Since this publication is germane to the topic and represents the baseline for our profession it is appropriate that we review their findings as it relates to the first 2 questions. They make it clear in their introduction that this was not a clinical practice guideline, formal evidence review, recommendation or evidence-based guideline. They suggest instead that this paper is intended to start a discussion on the topic. Their paper outlines the formation of the committee, their methods for the literature review and how they reached a consensus.

The first question they posed was “Is routine chemical prophylaxis for VTE warranted in foot/ankle surgery?” Their consensus statement was “Current evidence argues against the routine use of chemical prophylaxis for VTE in foot and ankle surgery or in injuries requiring immobilization.” Unfortunately, there is a risk that this statement may be interpreted that no patients undergoing foot and ankle surgery or injuries warrant therapy. This would be the lazy approach to this article. We should notice the word “routine” in their statement. This suggests that although not all foot ankle injuries or surgery would require prophylaxis, there are cases that should warrant it. Indeed, that is the case.

The second question asked was “Which patients are appropriate candidates for VTE chemical prophylaxis?” The consensus statement was “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. This involves weighing the risk and consequences of bleeding against those of developing VTE. Exactly what constitutes sufficient risk to warrant chemical prophylaxis is not clear. Factors associated with
the greatest risk include a personal history of VTE, active or recent cancer <6 months, a hypercoagulable state, and prolonged lower extremity immobilization >4 weeks.” Relative to cast immobilization, the consensus was “Despite the strong association between limb immobilization and heightened VTE risk, immobilization by itself is rarely enough to warrant the use of chemical prophylaxis. The panel agreed that the greatest concern is when immobilization is prolonged (>4 weeks), rigid, or coupled with other known risk factors.”

There were 15 secondary risk factors identified: Advanced age (>60 years), Obesity (>30 BMI), Family history of VTE, Use of oral contraceptive pill or hormone replacement therapy, Varicose veins, Diabetes mellitus or >1 comorbidity, Severe foot/ankle injury, Non-weightbearing, Hospitalization, Bed rest, Achilles tendon rupture, Ankle fracture, TAR, Hindfoot arthrodesis, and General anesthesia. Reviewing these risk factors, an elderly diabetic patient undergoing a triple arthrodesis would have 1 primary and 6 secondary risk factors if this was considered a severe foot/ankle injury. This is also assuming this patient is not obese and has no other primary or secondary risk factors. In their discussion, all of these risk factors are reviewed as reported in the literature. They suggest that although not all patients require prophylaxis, the podiatrist should attempt to stratify the risk of each case. This should be discussed with the patient and a decision reached between both parties with how to proceed.

**STRATIFYING AND CALCULATING RISK**

Risk of DVT can be calculated using several scoring systems. One system is the Caprini risk assessment score, which utilizes a point system to determine whether a patient should be prophylaxed postoperatively. However this system requires a 40-point questionnaire and blood work, making it a clinically cumbersome and difficult to assess risk.

Pannucci et al developed a risk model for VTE in postsurgical patients that involved 7 risk factors that were weighted in the model from 1 to 5 points (19). One point factors included age ≥60 years and BMI ≥40. A single 2-point factor was identified as male sex. Three-point factors included both a personal history of VTE and scpsis/shock/systemic inflammatory response syndrome. Family history of VTE was graded at 4 points. Current cancer was assessed 5 points. This model presents an 18-fold variation in VTE risk in postoperative patients. They recommend that this model may help with doctor-patient discussion regarding risk assessment of VTE. This model does not evaluate the risk of cast immobilization; however, it does outline important factors to consider in the surgical patient.

**L-TRIP(CAST)**

In 2015 Nemeth et al published an article outlining their efforts to develop the L-TRIP(cast) (Leiden-Thrombosis Risk Prediction for Patients With Cast Immobilization) prediction score for VTE in patients requiring lower extremity cast immobilization (20). Their research involved 3 separate clinical trials. The first involving 4,446 cases and 6,118 controls outlined in the MEGA study (21-23). They started with a full prediction model that contained 32 variables, 3 genetic factors, and 6 biomarkers. Once they had this model, they produced a restricted model to have the minimum number of predictors with maximum predictive value resulting in a model with 11 variables, 2 genetic factors, and 1 biomarker. Ultimately they defined a clinical model that did not require blood draw or assays. Their clinical model included 14 environmental factors. The clinical model was converted to the L-TRIP(cast) score by weighting and assigning numerical values to all of the variables in the clinical model. The models were then validated in 2 separate studies. The first was the VTE study in Leiden, Netherlands and Cambridge, UK with 784 cases and 523 controls (24,25) and a second in Milan with 2,117 cases and 2,088 controls (26). After comparing all 3 models in their validation studies they concluded that the L-TRIP(cast) score performed slightly better than even their full model. Therefore, they conclude it is unlikely that adding genetic factors or biomarkers would lead to higher accuracy of the predictive model.

The point values are as follows: Age ≥35 and <55 = 2 points; Age ≥55 = 3 points; Male = 1 point; Current use of oral contraceptives = 4 points; Cancer past 5 years = 3 points; Pregnancy or puerperium = 3 points; BMI ≥25 and < 35 = 1 point; BMI ≥35 = 2 points; Pneumonia = 3 points; Family history of VTE = 2 points (We also include personal history of VTE); Comorbidity (RA, CKD, COPD, MS) = 1 point (We also include DM, CHF, IBD, Lupus); Hospital admission last 3 months = 2 points; Bedridden last 3 months = 2 points; Superficial vein thrombosis = 3 points; Plaster cast complete leg = 5 points; Plaster cast knee with ankle not enclosed = 2 points; Plaster cast foot = 2 points; Plaster cast lower leg = 4 points.

The authors do list a table outlining the percent positive, sensitivity, specificity, and positive predictive value and negative predictive values for each score from 2 to 14. Based on these values they tentatively recommend using a score of 9 for identifying patients at high risk for VTE. This value gives a positive predictive value of 5.0% while only 0.8% of those with a score of less than 9 will develop VTE. In their patient cohorts 74.7% of patients casted had an L-TRIP(cast) score of 9 or greater. They recommend this as a guideline only and suggest that clinicians weigh the risk of bleeding with the risk of thrombosis.
**PROPHYLACTIC TREATMENT**

Once the decision to prophylaxis is made what are the options? The American College of Foot and Ankle Surgeons consensus statement addressed this the following way: “Which methods of prophylaxis are recommended for patients at risk for VTE?” The consensus statement was “A multimodal approach to VTE prophylaxis is recommended for patients at high risk. This includes addressing any modifiable risk factors, using mechanical prophylaxis, early mobilization, and considering the use of chemical prophylaxis. Low-molecular-weight heparin (LMWH) is effective at reducing the rate of clinically significant VTE and also is likely to reduce the rate of post thrombotic syndrome (PTS). There is currently insufficient evidence to support the use of aspirin as an isolated measure of prophylaxis in high-risk patients. Placement of inferior vena cava (IVC) filters are discouraged and should be reserved only for patients at highest risk (e.g., previous history of VTE) when chemical and mechanical prophylaxis are not options” (18).

The CHEST recommendations are the use of LMWH in preference to all the other forms of anti-coagulation they listed and to add intermittent pneumatic compression device (IPCD) during the hospital stay (17). They suggest extending therapy for 35 days. In patients who decline injections they recommend using apixaban or dabigatran. In patients with high bleeding risk they recommend IPCD or no therapy. They do not recommend IVC filter for patients that cannot be prophylaxed chemically or mechanically.

Enoxaparin (Lovenox) a LMWH is an inexpensive medication, and most health insurance companies will pay for its use. Enoxaparin has a reversal agent that can be used in the case of a major bleeding event. Protamine sulfate is used for reversal and 1 mg of protamine will neutralize 1 mg of enoxaparin. Enoxaparin is dosed 30 mg subcutaneously twice daily and initiated 12 to 24 hours after surgery.

Apixaban (Eliquis) is dosed 2.5 mg twice daily and initiated 12 to 24 hours after surgery. There is currently no reversal agent albeit there is one currently under study. The half life is 12 hours and the effects of apixaban persists for 24 hours or two half lives. There are no changes indicated for renal dosing. Apixaban is not indicated for patients with mechanical prosthetic heart valves.

Dabigatran (Pradaxa) is dosed 110 mg for the first day then 220 mg once daily thereafter in patients with CrCL >30 ml/minute. For those with ≤30 ml/minute, no dosing recommendations can be made. The half life of dabigatran is 12 to 17 hours and longer in renally impaired patients. Idarucizumab (Praxbind) is available to reverse the effects of dabigatran when emergency surgery is necessary. It is also contraindicated in mechanical prosthetic heart valves.

Ibrahim et al in a systematic review including over 1,000 patients found that sequential compression devices and foot pumps significantly reduced the risk of developing DVT in trauma patients (27). The article also found that foot pumps were more effective than SCDs, and they stressed the importance of patient education to increase patient compliance. Transitioning a patient to a CAM walker instead of a cast, and allowing range of motion may also help decrease the risk. Ted hose or compression stockings used to be recommended in prevention of DVT, however, Jin et al found no statistical significant difference in incidence of developing a DVT in patients that wore compression stockings versus those that did not (28). At the conclusion of the article, the authors reported that due to limited studies their article had some weakness, and according to the 2016 American College of Chest Physicians the use of compression stockings is recommended as they may at least aid in venous return and reducing swelling.

**DISCUSSION**

It is clear that not all foot and ankle surgery or cast immobilized patients require VTE prophylaxis and this would lead to poor medical practice and unnecessary treatment and cost. However, the inverse is also false. Failing to prophylax patients that are at high risk may lead to severe sequelae including death. This may be avoidable. There is no perfect solution to this conundrum, however, every practitioner should have this conversation with patients that are at increased risk.

In our practice we have a separate consent form (Figure 1) that is reviewed with all patients requiring cast immobilization or surgery since there are patients that are at high risk without intervention. Certainly surgical procedures that involve casting typically involve general anesthesia, longer length of surgery, and bed rest, significantly increasing their risks and the majority of these will have prophylaxis recommended to them.

We use a slightly modified version of the L-TRiP(cast) score (Figure 1). We consider personal history of VTE at the same level as family history of VTE. We also include diabetes, lupus, congestive heart failure, and irritable bowel disease or other comorbidities although they are not explicitly listed in the L-TRiP(cast) predictive model. Lastly we include hormone replacement therapy equal to oral contraceptive therapy. We typically recommend prophylaxis in most cases requiring Achilles tendon lengthening or repair. In these cases it is difficult to differentiate the source of calf discomfort whether it be from the injury or repair versus new onset DVT and some level of edema may be expected with the procedure. Additionally the primary pump for venous return in the calf is compromised in these cases.

We recommend enoxaparin as our first option since we have found it often difficult to get insurance company
In cases that require surgery of the Achilles tendon we may recommend clot prevention therapy. Be advised that the calf muscle is the primary pump to return blood flow in the veins and it will be compromised in these cases. In addition, pain and swelling will occur in this area and may be difficult to determine if a clot develops.

The preferred medical treatment for clot prevention is Lovenox or (enoxaparin generic). Lovenox requires twice daily injections. This medication is the less expensive option and more often covered by insurance. There is also a readily available reversal agent should we have a bleeding complication secondary to the medicine. That are increased risks of bleeding and adverse reactions that can occur with these medications.

If you are unwilling to inject yourself and your insurance company will cover the medicine an alternative route is Eliquis (apixiban generic) in the form of a pill by mouth. This medication is more expensive and not all insurance companies will provide it. The medicine has no reversal agent in cases of bleeding complications. It will last in your system for approximately 24 hours from the last dose.

Increasing motion or moving the ankle will reduce the risk. It is often not advised or possible immediately after surgery. Compression therapy may also help if no cast is required or after it is removed.

You are not required to take either medicine but we will make our recommendations based on the above table. There medications do add some bleeding risks and possible severe reactions if left untreated that can cause death. You are also, welcome to review your risks with your primary care physician or other provider prior to surgery.

PLEASE DO NOT USE EITHER MEDICATION BEFORE SURGERY. Please wait to start the medication at least 12 hours after the procedure but within the first 24 hours.

By signing here, you agree that this information has been reviewed with you and that you understand your options. You were allowed an opportunity to ask questions and they were answered to your satisfaction.

Patient or legal guardian: ____________________________
Dr. Stephan LaPointe: ____________________________

Figure 1. Blood Clot Risk Assessment and Consent.
approval for apixaban and it is recommended over the latter. In those unwilling to inject, we recommend apixaban for treatment although dabigatran is another option. We write the prescription for enoxaparin and/or apixaban but do not require the patient to use the medication as long as they understand the perceived risks. We typically continue to treat until the patient is no longer in a cast and is mobile, keeping in mind the recommendation from CHEST to continue treatment for 35 days. We discuss early mobilization or active dorsiflexion exercise to reduce the risk whenever possible.

Although we assess the risk with the LTRiP(cast) score and let the patients know that a score of 9 is the approximate cut-off for recommendation of anti-coagulation we make exceptions on either side depending on the patient’s circumstances. As an example a patient that has a personal history of VTE who is having a first metatarsophalangeal joint arthrodesis and scores a 7 due to BMI and age criteria does not require prophylaxis per their score. However, the patient may opt to have therapy due to prior poor experience. Others may opt not to treat. We do wish to educate everyone on their relative risk so that they can make an intelligent and informed decision.

REFERENCES

Premium Podiatric OTC Orthotics

Metatarsalgia  Pronation  Plantar Fasciitis

Even KIDS OTC orthotics!

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