ACFAS Clinical Consensus Statement

American College of Foot and Ankle Surgeons’ Clinical Consensus Statement: Risk, Prevention, and Diagnosis of Venous Thromboembolism Disease in Foot and Ankle Surgery and Injuries Requiring Immobilization

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Venous Thromboembolism Prophylaxis Clinical Consensus Statement Panel of the American College of Foot and Ankle Surgeons, Chicago, IL

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ABSTRACT

The purpose of this document is to provide guidance for physicians regarding the risk, prevention, and diagnosis of venous thromboembolism disease after foot and ankle surgery and while caring for lower extremity injuries that require ankle immobilization. A panel composed of all authors of this document reviewed the published evidence and, through a series of meetings, reached consensus regarding the viewpoints contained herein. We conclude that routine chemical prophylaxis is not warranted; rather, patients should be stratified and have a prevention plan tailored to their individual risk level. An effective venous thromboembolism prevention program is typically multimodal and focuses on addressing any modifiable risk factors, use of mechanical prophylaxis, early mobilization, and careful consideration of the use of chemical prophylaxis. The final decision regarding use and method(s) of prophylaxis adopted should be agreed upon by both the clinician and patient after a discussion of the potential benefits and harms as they relate to the individual. This should take place preferably during the preoperative visit or in the immediate post-injury setting, and it may need to be revisited during the course of care if the patient’s risk level changes. Prompt recognition of the signs and symptoms of deep venous thrombosis following surgery or injury is important. Patients suspected of deep venous thrombosis should receive further work-up with either a D-dimer test or duplex venous ultrasound of the symptomatic leg, depending on their pretest probability for the disease. The latter can be determined using a validated clinical decision-making tool (e.g., Wells criteria).

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Definition of Venous Thromboembolism Disease

For the purposes of this document, venous thromboembolism disease (VTED) is defined as a clinical spectrum of pathologic clotting that encompasses both deep venous thrombosis (DVT) and pulmonary embolism (PE). DVT is the formation of a thrombus in one of the deep veins of the body. PE is a blockage of one or more of the pulmonary arteries by a thrombus that has travelled from another part of the body via the deep venous system.

Background Rate of Venous Thromboembolism Disease

VTED affects 300,000 to 600,000 people and is the proximate cause of more than 60,000 deaths each year in the United States [1].

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There is potentially increased risk of VTED following foot/ankle surgery and lower limb injury; however, the incidence of VTED in these instances is poorly understood. This is at least partly due to the wide range of procedures/injuries encountered in this area of the body, their varying levels of complexity, and the varying aftercare protocols (e.g., immediate weightbearing versus strict non-weightbearing). In addition, thrombotic endpoints have not been consistently reported in the literature from study to study, and they vary from strictly clinical (i.e., symptomatic DVT) to sonographic and phlebographic, and they also vary in terms of reported location (e.g., distal versus proximal lower extremity DVT).

In a large administrative database study with nearly 90,000 patients, Jameson et al (2) found that the rate of symptomatic VTED after ankle fracture surgery, total ankle replacement surgery, hindfoot arthrodesis, or first metatarsal surgery was less than 0.3% for each type of surgery. Similarly, following 2,733 patients for an average of 90 days after foot or ankle surgery, Mizel et al (3) found that the prevalence of symptomatic DVT and non-fatal PE was only 0.22% and 0.15%, respectively. In contrast, Solis and Saxby (4) found a 3.5% incidence of post-operative DVT among 201 patients who underwent foot ankle surgery that involved use of venous sonography for surveillance. However, all of these DVT cases were clinically asymptomatic. Still other studies found alarmingly high rates of VTED following foot/ankle surgery. In particular, 2 reports of studies using phlebographic endpoints observed DVT rates among patients who had not received chemical prophylaxis to be as high as 28% and 36% following ankle fracture surgery (5) and Achilles tendon rupture surgery (6), respectively.

**Shortcomings of Current Guidance**

The American College of Chest Physicians (ACCP) (7) recommends use of chemical prophylaxis or an intermittent pneumatic compression device for patients undergoing major orthopedic surgery in their latest 2012 guidelines. The same guidelines suggest that no chemical prophylaxis is needed for patients with a lower extremity injury that requires immobilization (7). These guidelines, however, do not attempt to differentiate among the numerous foot and ankle conditions encountered in clinical practice and, instead, treat all isolated injuries distal to the knee in the same manner. Furthermore, ACCP panel members were asked only to consider the use of prophylaxis to reduce fatal and symptomatic PE and symptomatic DVT when developing their recommendations; the panel did not take into account the possible adverse outcomes associated with the development of postthrombotic syndrome (PTS). PTS is characterized by leg pain and swelling and occurs when venous valvular reflux and outflow obstruction develop after DVT (8). It is estimated that PTS may affect 20% to 50% of patients diagnosed with DVT, and most symptoms of PTS become apparent within 2 years of the diagnosis of DVT (9). PTS can lead to diminished quality of life and reduced productivity (10), and 5% to 10% of patients with PTS develop a severe form of illness, which may include venous leg ulcers (8.9). Recent work suggests that PTS avoidance can significantly reduce overall health care costs (11). Although we agree that avoiding symptomatic VTED and avoiding mortality in the short term remain the primary outcomes of interest when considering the use of chemical prophylaxis, our panel felt that PTS avoidance was also an important endpoint worthy of consideration when developing the viewpoints contained herein.

The purpose of this CCS is to address the topics of risk, prevention, and diagnosis of VTED following foot and ankle surgery or injury. More specifically, our aim is to provide insight into 4 questions:

1. Is routine chemical prophylaxis warranted after foot/ankle surgery or injury requiring immobilization?
2. If routine prophylaxis is not warranted, which patients should receive chemical prophylaxis?
3. Which method(s) of VTED prophylaxis is/are preferred?
4. Which diagnostic tests should be used for an individual suspected of DVT?

**Materials and Methods**

**Creation of Panel**

Members of ACFAS have suggested that CCSs would be useful; therefore, ACFAS enacted an initiative to create such documents for foot and ankle surgeons. This initiative was originally conceived to report on a variety of topics and take the place of previous clinical practice guidelines (CPGs). To move forward with this initiative, a formal consensus method process was undertaken. On April 18, 2014, experts in the field of foot and ankle surgery were sent an invitation by ACFAS to participate on a panel tasked with developing a CCS on VTED prophylaxis. The 6-member panel completed disclosures and was led by a chairperson and assisted by ACFAS staff. Over several months, panel members participated in e-mail dialogue, several conference calls, and a face-to-face meeting. The panel’s stated goal was to examine the current literature regarding the use of VTED prophylaxis and DVT diagnosis after foot and ankle surgery or injury, and to compile this information to provide direction in risk assessment, use of prophylaxis, and diagnosis of VTED in postoperative and post-injury settings. A literature search was undertaken to identify published studies on these topics. In addition, the panel reached consensus on a series of questions relating to VTED prophylaxis and diagnosis.

**Literature Review**

Search terms were identified for the 3 principal CCS areas of interest (i.e., VTED risk, VTED prevention, and diagnosis of DVT) and were searched within the Cochrane Database of Systematic Reviews, Cochrane Controlled Trials, PubMed, OVID, EMBASE, Cumulative Index of Nursing and Allied Health Literature (CINAHL), and Google Scholar. The search terms and Boolean operators utilized to identify articles relating to VTED risk were as follows: (“risk” OR “risk assessment” OR “incidence” OR “prevalence”) AND (“venous thromboembolism” OR “deep vein thrombosis” OR “pulmonary embolism” OR “postthrombotic syndrome”) AND (“foot” OR “ankle”). Studies involving elective surgery and trauma patients were included. Studies dealing primarily with multitrauma patients were excluded. The search strategy used to identify articles relating to VTED prevention was as follows: (“foot” OR “ankle”) AND (“immobilization” OR “cast” OR “orthosis” OR “surgical” OR “trauma”) AND (“venous thromboembolism” OR “deep vein thrombosis” OR “pulmonary embolism” OR “postthrombotic syndrome”) AND (“prophylaxis”) OR “thromboprophylaxis” OR “low molecular weight heparin” OR “LMWH” OR “aspirin” OR “mechanical” OR “inferior vena cava filter” OR “IVC filter”). Again, studies involving elective surgery and trauma were included, whereas studies dealing primarily with multitrauma patients were excluded. The search terms and Boolean operators used to identify articles relating to DVT diagnosis were as follows: (“diagnosis” OR “algorithms” OR “predictive value” OR “tests” OR “D-dimer” OR “Hohman’s test” OR “Hohman’s sign” OR “duplex venous ultrasound” OR “phlebography”) AND (“venous thromboembolism” OR “deep vein thrombosis”). Studies involving primarily emergency room or inpatient populations were excluded because the panel was interested in determining the most appropriate methods for diagnosing DVT in the outpatient setting.
A manual review of the bibliographies of candidate studies was performed to identify additional articles. Candidate articles and abstracts were evaluated by 2 panel members and agreed upon by the chair and other panel members for final inclusion in the body of evidence. We used existing, current, systematic reviews and other level 1 and 2 evidence studies that dealt specifically with foot/ankle surgery or injury as the basis of evidence (Supplemental Appendix SA). Lower-level evidence articles and articles from other medical disciplines including general surgery, general orthopedics, and internal medicine were used when gaps in the foot/ankle literature existed. Position statements (12) and guidelines (7,13,14) from other organizations were also considered. Ultimately, 43 high-level evidence articles (2–6,15–52), which included seven systematic reviews, served as the principal source of evidence (Supplemental Appendix SB).

Consensus

The viewpoints contained herein were formulated by integrating the available evidence with expert opinions of the panel members. To this end, a modified Delphi method was utilized to help attain consensus on several pertinent clinical questions (53). A series of 22 statement questions were developed by the panel chair with panel member input. These were sent to all panel members to determine relevancy, whether they should be included, and categorization. Once the questions were finalized, they were reviewed and answered by all panel members. The answers were in the form of Likert scale (54) (Supplemental Appendix SC). Ultimately, 43 high-level evidence articles (2–6,15–52), which included seven systematic reviews, served as the principal source of evidence (Supplemental Appendix SB).

Results and Discussion

The panel was able to reach consensus on each of the 22 questions (Supplemental Appendix SD). These responses served as the major points of discussion contained herein.

Is Routine Chemical Prophylaxis for VTED Warranted in Foot/Ankle Surgery or in Injuries Requiring Immobilization?

Consensus Statement: Current evidence argues against the routine use of chemical prophylaxis for VTED in foot and ankle surgery or in injuries requiring immobilization.

The panel agreed that routine use of chemical prophylaxis is not warranted, given the relatively low incidence of serious VTED events and the inherent bleeding risks associated with the use of chemical prophylaxis. This differs from hip and knee replacement surgery, where the risk of symptomatic DVT may be as high as 50% without effective prophylaxis and the risk-benefit ratio frequently tips in favor of chemical prophylaxis use (7). Furthermore, most cases of DVT following foot/ankle surgery or injury are isolated, asymptomatic calf thrombi (35). Although the general literature suggests that as many as 20% to 30% of distal DVT may extend into the more proximal veins and become a threat for PE (55–57), the foot and ankle literature does not seem to bear this out (2,4,18,22). Using the English National Health Service and Kaiser Permanente Northwest databases (N = 110,282 patients with 3 to 6 months of follow-up), the rate of symptomatic and/or proximal VTED following foot and ankle surgery was assessed as less than 0.3% (2,18,22). Finally, although PTS is a recognized and preventable consequence of symptomatic lower extremity DVT, the panel agreed that the literature is not as convincing with regard to the role of asymptomatic, distal DVT in the development of PTS (58–60).

Which Patients Are Appropriate Candidates for VTED Chemical Prophylaxis?

Consensus Statement: 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 risks and consequences of bleeding against those of developing VTED. Exactly what constitutes sufficient risk to warrant chemical prophylaxis is not clear. Factors associated with the greatest risk include a personal history of VTED, active or recent cancer, a hypercoagulable state, and prolonged lower extremity immobilization.

Although graded risk assessments (e.g., the Caprini risk model) have been developed (61–63) and validated for use in hospitalized patients and in select surgical specialties (64,65), none have been validated for use in foot and ankle surgery or injury. However, most studies identify a common set of risk factors for VTED, which can be categorized broadly as follows:

1. Patient-specific
2. Related to the treatment course
3. Related to the surgery or injury itself

Risk factors identified by the panel as being most important in foot/ankle disorders are shown in Table 1. When one or more primary risk factor is present, clinicians should consider a multimodal approach to VTED prophylaxis that may include the use of chemical prophylaxis. If no primary risk factors are present, careful consideration can be given to the presence of any secondary risk factors and their severity. These predisposing factors are seldom sufficient by themselves to justify the use of chemical prophylaxis. However, secondary risk factors or combinations thereof can have important implications for the type and duration of VTED prophylaxis and should be reviewed to assess the overall risk for each patient.

Primary Patient-Specific Risk Factors

Personal history of VTED (15,18,20,44,61–63,66), hypercoagulability (44,62,63,67–69), and current or recent cancer (17,44,61,66,70) are among the strongest risk factors for VTED and warrant special consideration.

Personal History of VTED

A personal history of VTED is recognized as perhaps the single most important risk factor for a subsequent VTED event. Examining 665 patients who underwent ankle replacement surgery, Barg et al (15) found that patients with previous VTED were 7 times more...

...
likely (multivariate odds ratio [OR] 7.1, 95% confidence interval [CI] 2.9 to 17) to develop DVT compared with those without previous VTED. Felcher et al (18) found that history of VTED conferred a 13 times greater risk (multivariate OR 23, 95% CI 9.0 to 58) of subsequent VTED event among 7,264 patients who underwent foot surgery. In their examination of a cohort of 602 foot and ankle surgery patients, Hanslow et al (20) also found that previous VTED was one of only a handful of risk factors for postoperative VTED event. Looking outside the foot/ankle literature, Beam et al (66) found that prior history of VTED was the strongest predictor of 12 variables evaluated in their multivariate model for predicting subsequent VTED event among 7,940 patients presenting to the emergency room with symptoms of VTED. Edmonds et al (44) also discovered a 6 times greater risk (multivariate OR 2.6, 95% CI 1.0 to 6.8) of developing postoperative DVT among general surgery patients who had a prior history of DVT. Finally, several widely used graded VTED risk assessments place “personal history of VTED” in the highest risk stratum (61–63).

**Hypercoagulability**

Although hypercoagulability is only sparsely mentioned in the foot/ankle specific literature, the panel agreed that the presence of a hypercoagulable state, whether inherited (e.g., antithrombin III deficiency, protein C or S deficiency, factor V Leiden mutation, dysfibrinogenemia, homocysteinemia, and 20210A prothrombin mutation) or acquired (e.g., antiphospholipid antibodies, Lupus anticoagulant, myeloproliferative disorders, disorders of plasminogen and plasmin activation, hypercoagulability syndromes, and homocysteinemia) should be regarded as a strong risk factor for VTED, given the abundant evidence in the general literature. Several high-quality studies indicate that factor V Leiden mutation is probably the most pertinent of the hypercoagulable states. The presence of factor V Leiden mutation confers a 7 to 79 times greater risk (heterozygous versus homozygous) for DVT, and it is associated with 20% of all VTED events (44,67–69). Furthermore, several graded risk assessments assign a high risk value to hypercoagulability (62,63). It is important to recognize that routine screening before surgery is not currently recommended, even though hypercoagulability is considered a strong risk factor for VTED. A specialist’s advice should be sought before screening is considered.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Risk factors for venous thromboembolism disease during management of foot and ankle conditions</th>
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<tbody>
<tr>
<td><strong>Patient Specific</strong></td>
<td><strong>Treatment Specific</strong></td>
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<tr>
<td>Personal history of VTED</td>
<td>Immobilization &gt;4 wk</td>
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<tr>
<td>Hypercoagulability</td>
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<tr>
<td>Active/recurrent (&lt;6 mo) cancer</td>
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**Secondary Patient-Specific Risk Factors**

The panel identified the following patient-specific factors as also being important during VTED risk assessment: obesity (4,15,18,35,37,44,61–63), advanced age (4,16,27,37,40,66), oral contraceptive pill or hormone replacement therapy (OCP/HRT) use (18,44,72,73), family history of VTED (44,61,62,67,68), varicose veins (44), higher injury severity score (33,35,37), and diabetes mellitus or the presence of more than one comorbidity (2,22,40,43). Variables for which there is insufficient evidence supporting their role as risk factors include smoking, gender, race/ethnicity, pregnancy, and cardiovascular factors (44). Although population-based studies have identified smoking as a risk factor in the general population (74–76), studies in surgical patients suggest that smoking has either no effect (16,43) or a “protective” effect (44,77) on the development of postoperative VTED. However, clinicians should have a heightened awareness in patients who smoke and use oral contraceptives, as these may act synergistically to increase VTED risk (78).

**Obesity**

Barg et al (15) found that obesity, defined as body mass index (BMI) >35 kg/m², was an independent risk factor for DVT after total ankle replacement surgery (multivariate OR 6.9, 95% CI 2.2 to 22). Felcher et al (18) also noted a similar but somewhat smaller increase in risk among obese (BMI >30 kg/m²) patients undergoing foot surgery (multivariate OR 2.6, 95% CI 1.0 to 6.8). Similarly, Solis and Saxby (4) found that BMI was associated with an increased risk of occlusive DVT in their cohort of patients undergoing various types of foot and ankle surgery. In a recent systematic review, Schade and Roukis (13) concluded that obesity was an important risk factor for VTED when treating foot/ankle conditions, as did Edmonds et al (44) in their meta-analysis of risk factors for DVT following general surgery. Using a BMI threshold of 40 kg/m², Shibuya et al (37) also recognized obesity as an important risk factor for VTED following isolated foot or ankle trauma (DVT: multivariate OR 2.4, 95% CI 1.3 to 4.1; PE: multivariate OR 3.1, 95% CI 1.6 to 5.6). Several widely used graded risk assessments also frequently include obesity as a risk factor (61–63). Although considerable evidence indicates that obesity, using its most practical definition (BMI >30 kg/m²), is associated with higher VTED risk following foot/ankle surgery or injury, the panel agreed that the variability in definitions and lack of an association reported in some

Current or Recent Cancer

Patients with active or recent cancer are at particularly heightened risk for VTED. Lin et al (70) found that the rate of DVT following orthopedic surgery in the tibia and fibula among patients with cancer and receiving appropriate VTED prophylaxis was as high as 12.5%. Among patients not receiving chemical prophylaxis, Saragas et al (17) found that active or previous malignancy was present in 27.3% of those who developed VTED after foot or ankle surgery compared with only 11.7% of their non-VTED patients. Turning to general surgery, Edmonds et al (44) demonstrated that cancer conferred nearly a 3 times greater risk of developing postoperative DVT (pooled OR 2.9, 95% CI 2.0 to 4.3). Similarly, looking at nearly 8,000 patients who presented to the emergency department with symptoms resembling VTED, Beam et al (66) found that active malignancy conferred a 2 times greater risk of actually having VTED (multivariate OR 2.2, 95% CI 1.6 to 2.9). Furthermore, Panucci et al (61) recently published a validated graded risk model for predicting 90-day VTED events in postoperative patients, and “current cancer” occupies their highest risk stratum. Because tumor cells are thought to be responsible for the activation of blood coagulation seen in cancer patients, the risk of VTED is likely no longer present in patients who have been in remission for more than 6 months (71).
foot/ankle studies (2,22,33,40) make it difficult to fully quantify the magnitude of its effect.

**Advanced Age**

Advanced age is a frequently cited risk factor for VTED. Radl et al (16) reported a mean age of 61.7 years in patients who developed DVT after hallux valgus surgery compared with 48.4 years in patients who did not develop DVT. Although risk estimates were not reported, patients older than 60 years of age were found to have a statistically significant greater risk of developing DVT. Using a large administrative database, Soohoo et al (40) found that being aged 50 to 75 years as compared with younger than 50 years predisposed individuals to VTED among 57,183 patients undergoing ankle fracture surgery (DVT: multivariate OR 3.4, 95% CI 1.1 to 10; PE: multivariate OR 1.9, 95% CI 1.2 to 2.9). Makhdom et al (27) and Solis and Saxby (4) also observed that DVT rates increased significantly in older age groups after foot and ankle surgery. Riou et al (33) also reported that an age older than 50 years was an important predictor of VTED among a cohort of 2,755 patients treated conservatively for isolated injuries to the lower limb (multivariate OR 3.1, 95% CI 2.2 to 4.3). Among patients who sustained isolated foot or ankle trauma, Shibuya et al (37) found that risk of VTED increased by 20% for each decade of age. The general literature also recognizes advanced age as an important risk factor for DVT among immobilized patients (44,66). Although cut-points are often drawn for reporting purposes, it is important to recognize that VTED risk increases progressively with age.

**Oral Contraceptive Pill and Hormone Replacement Therapy**

Fletcher et al (18) noted that the use of oral contraceptive pill and hormone replacement therapy (OCP/HRT) conferred a 4 times increased risk of VTED following foot surgery (multivariate OR 4.0, 95% CI 1.3 to 12.8). Edmonds et al (44) also concluded that OCP use increased the risk of postoperative DVT among general surgery patients (pooled OR 2.5, 95% CI 1.5 to 4.0). A recent Cochrane review found an increased risk of VTED in women using combined OCP compared with those not using OCP in the general population (pooled relative risk [RR] 3.5, 95% CI 2.9 to 4.3) (72). The actual risk varied according to estrogen dose and type of progestogen. Similarly, HRT has been found to increase the risk of DVT by 2 to 3 times, with the risk highest during the first year of use (79). The increased risk with HRT is also noted in men receiving estrogen therapy for prostate cancer (79).

**Family History of VTED**

Family history of VTED is a natural factor to consider, given the significance of inherited blood disorders in VTED. Multiple references highlight the importance of assessing family history when assessing VTED risk (44,67,68). In terms of validated graded risk assessments, Caprini (62) placed family history in the same risk stratum as hypercoagulability and personal history of VTED, and Pannucci et al (61) placed family history in the second highest risk stratum, just below current cancer and above personal history of VTED. Caprini (62) further suggested that family history is probably the most commonly overlooked risk factor for VTED.

**Varicose Veins**

Varicose veins are an indication of underlying valvar insufficiency and venous stasis, which likely contributes to the higher rate of DVT seen in this population. Although this claim is somewhat controversial and not supported in all studies (33), the summation of current evidence in the surgical literature suggests that the presence of varicose veins is associated with a 2 to 3 times greater risk for VTED (pooled OR 2.4, 95% CI 1.7 to 3.4) (44).

**Higher Injury Severity Score**

A recent systematic review specific to foot and ankle disorders identified severe foot injury as an important risk factor for VTED (35). Shibuya et al (37) found that a higher injury severity score (ISS) was independently associated with a greater likelihood for development of VTED among patients with isolated foot or ankle trauma (multivariate OR 1.2, 95% CI 1.1 to 1.3, for each unit increase in ISS). Riou et al (33) also reported that severe foot/ankle injuries (defined as injuries involving a fracture, dislocation and/or complete tendon rupture) were associated with increased risk for VTED compared with non-severe injuries (multivariate OR 1.9, 95% CI 1.3 to 2.6). These findings may be explained by a greater amount of disruption to the lymphatic and venous systems that is expected in more severe foot/ankle injuries. Although this risk factor has not been studied in great detail, the panel agreed that the narrow confidence intervals and large number of subjects studied (N = 49,254) makes this an important concern when assessing VTED risk.

**Diabetes Mellitus or More Than One Comorbidity**

Several large studies have identified that patients presenting for operative (2,40) or nonoperative (22) management of ankle fractures are at increased risk for developing VTED when they have more than one comorbidity or the presence of diabetes mellitus. In one study (2), non–insulin–dependent diabetes mellitus, in particular, was found to have a greater effect on VTED risk in patients undergoing ankle fracture surgery (multivariate OR 15, 95% CI 9.6 to 22). In their study of a prospective cohort and somewhat smaller population that was immobilized for ankle fractures, Yi et al (43) also identified an increased risk for DVT among patients with diabetes mellitus.

**Primary Risk Factors Related to Treatment Course**

Prolonged limb immobilization (>4 weeks) confers the greatest risk for VTED among the many factors encountered during the treatment course (3,4,17,20,21,33,35). Immobilization, as it relates to the foot and ankle, refers to the use of a splint, cast, boot, external fixation or other device, or the physical state of the patient (e.g., arthrodesis, neuromuscular contracture) that prevents normal movement across the foot and/or ankle joints.

**Prolonged Immobilization**

Compelling evidence indicates that prolonged immobilization is a critical factor in the development of VTED following foot and ankle surgery or injury. Immobilization and non-weightbearing, for example, were the only predictors of postoperative VTED identified by the often cited study of Mizel et al (3). Lapidus et al (5) found that cast immobilization increased the rate of postoperative VTED after ankle fracture surgery by more than 3-fold compared with the use of an ankle orthosis alone. Hanslow et al (20) found that immobilization after foot or ankle surgery significantly increased the risk for VTED, whereas non-weightbearing alone did not. Studying a large group of patients receiving nonsurgical care for isolated injuries below the knee, Riou et al (33) found that rigid immobilization conferred a nearly 3 times greater risk of VTED (multivariate OR 2.7, 95% CI 1.6 to 4.4). It is important to recognize that rigid immobilization of the limb—particularly of the ankle joint—is what drives the increased risk for VTED. Using a cohort of nearly 8,000 patients presenting to the emergency department with symptoms resembling thromboembolism, Beam et al (66) found that a recent history of limb immobilization (multivariate OR 2.2, 95% CI 1.4 to 3.6) conferred the greatest risk of VTED among several other forms of immobilization (e.g., neurologic, travel, bed rest). Despite the strong association between limb immobilization and heightened VTED risk, limb 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.

Secondary Risk Factors Related to Treatment Course

Non-weightbearing status (3,15,33,35), hospitalization (1,14,76,80–82), and bed rest (76) were recognized as secondary risk factors associated with the development of post-injury/surgery VTED. Because most foot and ankle surgery today is performed in an outpatient setting, there were few reports in the foot/ankle specific literature to draw upon regarding hospitalization and bed rest; therefore, these opinions were mostly formulated using the general literature.

Non-Weightbearing Status

In a recent systematic review (35), non-weightbearing status was identified as an important risk factor for VTED during surgical and conservative management of foot and ankle conditions. Riou et al (33) found that non-weightbearing status was one of four significant risk factors for VTED in their observational study of nearly 3,000 patients with isolated below-knee injuries treated without surgery (multivariate OR 4.1, 95% CI 1.7 to 9.9). Mizel et al (3) demonstrated a statistically significant relationship between VTED and treatment regimens that included non-weightbearing, although admittedly the increase in risk was very small (RR 1.004, P= .01). Finally, Barg et al (15) found that patients who were not fully weightbearing after total ankle replacement surgery were also at increased risk for postoperative DVT (multivariate OR 4.5, 95% CI 1.8 to 11).

Hospitalization

Hospital confinement has long been recognized as a risk factor for VTED (1,81). In fact, nearly two thirds of all VTE in the United States are believed to occur during or around the time of hospitalization (80). It is important to recognize that most hospitalized patients have at least one risk factor for VTED, and approximately 40% will have three or more risk factors due to their past medical history, general acuity, and/or treatment care plan established by their surgeon (82). Consistent with other major organizational guidelines, the panel agreed it is prudent to consider patients who have been hospitalized for more than 24 hours to be at high risk for VTED until discharge, and patients hospitalized for more than 72 hours to be at somewhat higher risk for VTED subsequent to discharge (7,14).

Bed Rest

Bed rest is often used as an adjunct treatment for patients with foot and ankle disorders. The term may apply to patients in the hospital, patients who have temporary or long-term stays at a nursing facility, or outpatients at home. At least one population-based, case-control study (76) with 1,250 participants not restricted to foot and ankle surgery identified that hospital, nursing home, or other chronic care facility confinement was an independent risk factor for VTED (multivariate OR 8.0, 95% CI 4.5 to 14).

Secondary Risk Factors Related to Anesthesia, Surgery, or Injury Type

The panel recognized the following risk factors for VTED that relate to the surgery or injury itself: general anesthesia (44,83) (versus regional or monitored anesthesia care), operative and nonoperative management of ankle fractures (2,5,22,31,32,36,40,43), operative and nonoperative management of Achilles tendon ruptures (2,21,27,29,30,34), hindfoot arthrodesis (2,4), and total ankle replacement surgery (2,15,84). It is unclear whether tourniquet use (3,4,17,20,35,38,85) (including dependence on location or duration) or arthroscopic surgery (7,62) pose any significant excess risk for VTED. It is unlikely that hallux valgus surgery and treatment of metatarsal fractures alter VTED risk appreciably (2,16,18,39).

General Anesthesia

Among general surgical patients, Edmonds et al (44) found that general anesthesia conferred nearly 3 times greater risk of developing postoperative DVT compared with regional anesthesia (OR 2.9, 95% CI 1.7 to 4.8). This can be explained by the observation that veins dilate approximately 22% to 28% in patients undergoing general anesthesia, leading to venous stasis—one of three conditions in Virchow’s triad that is necessary for the development of VTE (83). Venous dilation by as much as 57% may occur in patients receiving one liter of saline during general anesthesia, which may further increase the risk for VTED (83).

Surgery or Injury Type

The panel was of the general opinion that VTED risk increases with proximity of the injury or surgery to the knee, as previously noted by ACCP (82). Using the English National Health Service database (88,241 patients), Jameson and colleagues (2) demonstrated that the rates of VTED are 8 to 17 times higher than the general background risk following hindfoot arthrodesis and ankle fracture surgery, and 2 to 3 times higher after total ankle replacement surgery. The key concern is the prolonged ankle immobilization that often accompanies rearfoot and ankle surgery; however, events related to the injury or surgery itself (e.g., loss of the calf muscle pump in the case of Achilles ruptures, extensive soft tissue dissection in the case of ankle replacement surgery) likely contribute additional risk.

Solis and Saxby (4) identified that hindfoot surgery increased the risk for postoperative DVT, including occultive DVT, in a prospective cohort using sonography for surveillance. Similarly, using an administrative database of more than 7,000 patients undergoing hindfoot arthrodesis surgery, Jameson et al (2) found that hindfoot arthrodesis increased the risk for clinically significant postoperative VTED compared with background risk. Mizel et al (3) failed to show a difference in rate of VTED when comparing surgery level/type; however, their study had a very small number of total VTE events and contained significantly fewer hindfoot procedures (n=493) compared with the Jameson et al study (2).

Ankle fractures carry increased risk for VTED, whether managed conservatively or operatively. The incidence of VTED in ankle fractures treated with immobilization alone and without chemical prophylaxis ranges from 0.6% using a strictly clinical endpoint (36) to 5% using sonography (31). Similarly, the incidence of symptomatic VTED following ankle fracture surgery without chemical prophylaxis may be as high as 2.7% (32), while the rate of developing asymptomatic, calf thrombi is as high as 28% (5). Patients with multiple comorbidities (2,22,40), diabetes mellitus (2,43), advanced age (40), multiple risk factors (32), and/or open fractures (40) are at an even greater risk for VTED when presenting with ankle fractures. A delay in getting the patient to surgery may also increase VTED risk (43).

Achilles tendon ruptures are frequently associated with lower extremity DVT development. In fact, distal, asymptomatic thrombi may occur in up to one third of these patients (6,29). Although one study looking at an administrative database placed the incidence of symptomatic VTED at 0.8% (30), other studies suggest that clinically significant VTED will be observed in 6% of Achilles tendon ruptures regardless of management (operative or nonoperative) (21,34). It is important to recognize that it is likely the injury itself and loss of the calf muscle pump, and not the surgery itself, that confers the added risk for VTED. In fact, despite a higher overall incidence of major complications, patients undergoing operative repair of ruptured tendons have a 4 times lower incidence of DVT than those treated...
with nonoperative management (86). This result is not surprising, as patients with surgical repair are expected to regain function of their calf muscle pump faster and typically return to work earlier than those treated conservatively (87). Despite the high incidence of VTED with Achilles tendon ruptures, routine chemical prophylaxis is currently not recommended for these injuries (27,29,30). Instead, discretion should be left to the physician and patient, and should account for the presence of any other risk factors and, especially, the proposed rehabilitation protocol (e.g., early mobilization/weight-bearing versus prolonged cast immobilization). Persson et al (88) observed a 10% incidence of PTS at 7-year follow-up in patients with primarily distal DVT after surgery for Achilles tendon ruptures, suggesting that the avoidance of even distal, asymptomatic thrombi may be a desirable aim in this population.

The risk of VTED following total ankle replacement (TAR) surgery is also elevated (2,15,84). Evidence from one high-level study suggested that the incidence among patients undergoing TAR and receiving chemical prophylaxis is 3.9% (15). Similarly, a systematic review of primarily low-quality studies in patients who underwent TAR surgery found that the incidence of VTED ranged from 0.8% to 9.8% among studies reporting a VTED event (84). Thirteen of the 31 studies did not have a VTED event in their series, although use of chemical prophylaxis and use of clinical endpoints only may have attributed to this absence. In a large cohort involving 655 patients who underwent TAR surgery, Barg et al (15) recognized that obese patients (BMI >35 kg/m²), patients not fully weightbearing initially postoperatively, and patients with prior history of VTED were at highest risk for VTED postoperatively. These factors have each been identified as important risks elsewhere in this CCS, but they may warrant special attention among the TAR population.

**Which Methods of Prophylaxis Are Recommended for Patients at Risk for VTED?**

**Consensus Statement: A multimodal approach to VTED 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 VTED and also is likely to reduce the rate of 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 is discouraged and should be reserved only for patients at highest risk (e.g., previous history of VTED) when chemical and mechanical prophylaxis are not options.**

**Multimodal VTED Prophylaxis Program**

An effective multimodal approach to VTED prophylaxis involves 4 general strategies. First, the clinician must address the patient’s modifiable risk factors for VTED. In high-risk patients, for example, discontinuation of OCP/HRT 4 weeks prior to surgery (14) can be discussed. Plans for alternate contraception during this time may be necessary. Limiting the duration of hospital stay and bed rest requirements may also be promoted. Consideration may be given to performing surgical procedures under regional or local anesthesia rather than general anesthesia. Second, use of intermittent pneumatic compression, when possible, and liberal use of graduated compression stockings should be promoted to reduce postoperative and post-injury VTED. In patients who underwent orthopedic or general surgery, the use of graduated compression stockings was found to reduce the risk of DVT by 67% (pooled OR 0.33, 95% CI 0.26 to 0.41) (89). Third, early rehabilitation and mobilization of the limb should be encouraged, as this will help to re-engage the calf muscle pump through early weightbearing and ankle exercises (90). Use of removable devices, rather than rigid casts, can also allow for early foot and ankle range of motion (ROM) exercises during recovery. When casts are required, gentle exercises allowing for isometric contraction of muscles beneath the cast have been shown to increase peak popliteal venous velocities and may be an option for some patients (45). Minor modifications to surgical procedures, such as the use of rigid internal fixation, locking plates, and soft tissue anchors, also may allow for earlier ROM exercises and earlier weightbearing following procedures that have historically required prolonged immobilization. Finally, the use of chemical prophylaxis may be appropriate as part of a multimodal prophylaxis program for patients deemed to be at high risk for VTED.

**Low-Molecular-Weight Heparin**

The decision to use chemical prophylaxis should be based on each patient’s unique risk-benefit analysis and should involve carefully weighing the risks and consequences of bleeding against those of developing VTED. Low-molecular-weight heparin (LMWH) is effective in reducing the rate of clinically significant VTED and also likely reduces the rate of PTS. A 2014 Cochrane database review (46), which included 6 randomized controlled trials (RCT) and a total of 1,490 patients (5,6,23–26), found that LMWH reduced the risk of VTED by 50% in surgical and nonsurgical patients requiring lower leg immobilization. The risk reduction was even greater for nonsurgical patients (pooled OR 0.35, 95% CI 0.19 to 0.62) than for those patients who underwent surgery (pooled OR 0.54, 95% CI 0.37 to 0.80). However, LMWH clearly has the potential to cause harm, even though studies specific to foot/ankle surgery suggest that the risk is generally low (35). Thrombocytopenia, a potentially fatal complication, was reported in 3 patients (0.5%) undergoing TAR surgery (15). This resolved when LMWH was discontinued. Testor-oote et al (46) also found that 2 of 750 patients (0.26%) receiving LMWH experienced a major bleeding event, whereas minor bleeding events were reported in up to 8% of patients in the treatment group. Minor and major adverse events can substantially increase patient morbidity and overall cost of care. For this reason, clinicians may recognize that the risks and consequences of bleeding outweigh the benefits of LMWH use. Other more common issues relating to LMWH use include inconvenient daily injections, the need for staff availability for teaching, and medication costs. When chemical prophylaxis is needed and LMWH cannot be used, use of oral anticoagulants should be considered and blood monitoring may be required.

**Aspirin Use and Other Oral Anticoagulants**

No high-level evidence was found that addressed the issue of aspirin use in foot/ankle disorders. However, one retrospective comparative study using a consecutive series of 2,654 patients undergoing elective foot and ankle surgery was identified (91). In their study, Griffiths et al (91) determined that aspirin use (75 mg/d) was ineffective in altering the rate of postoperative VTED (0.47% in the aspirin group vs. 0.39% in the no aspirin group, p = .985). For these reasons, the panel agreed that there is insufficient evidence to support the use of aspirin as an isolated measure of prophylaxis in high-risk patients. Even though aspirin was included in the latest ACCP guidelines as an option for prophylaxis in hip fracture and hip/knee replacement surgery, it is important to recognize that ACCP estimated that the protective effect gained with aspirin (over placebo) is only modest and that LMWH shows greater relative efficacy for preventing VTED compared with aspirin (7). Furthermore, the National Institute for Health and Care Excellence (NICE) guidelines (14) do not regard aspirin and other antiplatelet agents as adequate prophylaxis for VTED. The panel agreed that when subcutaneous injections are not
an option in the outpatient setting (e.g., due to intolerance for self-injecting or likely patient nonadherence) and chemical prophylaxis is desired, warfarin with a target international normalized ratio (INR) of 2.5 (range 2.0 to 3.0) or newer oral agents such as apixaban, dabigatran, or rivaroxaban that do not require INR monitoring would be preferred to aspirin therapy.

Timing and Duration of Chemical Prophylaxis

When using LMWH, therapy should be started within 12 to 24 hours of surgery and ideally continued for the duration of immobilization. There is no obvious benefit to starting chemical prophylaxis preoperatively rather than postoperatively. At least one systematic review in the general orthopedic literature suggested that starting LMWH 12 hours postoperatively is as effective in preventing DVT as starting it 12 hours preoperatively (92). Although initiating chemical prophylaxis 12 hours postoperatively was the preferred timing among panel members, it may be reasonable to wait 24 hours or longer before the first administration of LMWH when surgical site hematoma is a concern. When initiating LMWH following a foot or ankle injury, therapy should begin around the same time that immobilization is instituted. With respect to duration of chemical prophylaxis in foot and ankle conditions, the panel agreed that continuing chemical prophylaxis for the duration of immobilization likely offers the best protection against VTED. This is because most studies involving limb immobilization continued chemical prophylaxis until the ankle could be moved again or the patient was weightbearing (5,6,23–26). Nevertheless, the actual duration should be tailored to each patient and should take into account the individual’s risk for VTED, bleeding risk, and any concurrent use of other VTED prophylaxis measures.

Inferior Vena Cava Filter

Use of an IVC filter has been suggested for patients with a history of VTED and contraindications to chemical and mechanical prophylaxis. However, ACCP cautioned that IVC filter efficacy for patients without a prior history of DVT is not well established (7). Given the relatively high potential for adverse events to occur during IVC filter placement, during the clinical course, upon retrieval, and in the long term, the risk-benefit balance tips toward definite harm for most patients (7). Specialist consultation is recommended prior to consideration of IVC filter placement.

Which Diagnostic Tests Should Be Obtained in a Patient With Suspected DVT?

Consensus Statement: When clinical suspicion of lower extremity DVT exists, the patient’s pretest probability for DVT should first be established, preferably using a validated clinical decision-making tool (e.g., Wells criteria). Obtaining a D-dimer level is an option for patients with a low pretest probability and is sufficient to rule out DVT if the test result is negative. A full leg venous duplex ultrasound of the suspected limb is recommended for patients with a moderate or high pretest probability of DVT or patients with a positive D-dimer test result.

Prompt recognition of DVT in the outpatient setting is essential, as the consequences of misdiagnosis can be serious and potentially fatal. Because only a minority of patients evaluated for suspected DVT have the disease (48), effective diagnostic strategies must be able to safely rule out DVT when it is absent and correctly rule in DVT when it is present. The panel recommends the following sequence of testing when determining the probability of DVT (Fig): First, determine the clinical probability (also referred to as the pretest probability), preferably by using a validated clinical decision-making tool (eg., Wells criteria). Next, obtain either a D-dimer assay for patients with a low pretest probability or a venous ultrasound study for those with moderate or high pretest probability (13). A venous ultrasound will also be warranted in low-risk patients with a positive D-dimer test result (13).

Wells et al (93) first reported criteria to determine pretest probability for the presence of DVT among a group of ambulatory outpatients in 1995. Their multicenter study evaluated 529 consecutive patients with clinically suspected DVT who had symptoms for less than 60 days. DVT was diagnosed in 84.7% (72/85) of patients determined to have a high pretest probability, in 32.9% (47/143) of patients with a moderate or high pretest probability, in 32.9% (47/143) of patients with a moderate pretest probability, and...
in only 5.3% (16/301) of patients with a low pretest probability. This report led to the development of the Wells clinical decision-making rule (also called the Wells score or the Wells criteria), which was later adapted and validated and is now widely used as the first step in diagnosing DVT. Low pretest probability is defined as a score of 0 or less, moderate risk is defined as a score of 1 to 2, and high risk is defined as a score of ≥3 (48) (Table 2). In a recent meta-analysis, which included 22 studies that utilized Wells criteria to aid in the diagnosis of DVT, Goodacre et al (51) found the pooled likelihood ratio (LR) for a high-risk score was LR 5.2, 95% CI 4.0 to 6.0, while the pooled LR for a low-risk score was LR 0.25, 95% CI 0.21 to 0.29. The study also found that individual clinical tests and features (e.g., calf pain, Homans’s sign) were of limited value in diagnosing DVT and that assessment of clinical probability with Wells criteria was more useful.

Once a patient’s pretest probability is determined, the next step is to decide whether D-dimer testing or venous duplex ultrasonography is needed. Patients with low clinical probability can be ruled out for proximal and distal DVT with a negative D-Dimer test result (51,52,94–96). This is true even in the postsurgical and post-injury settings where false positives may be more likely with D-dimer testing but the negative predictive value remains unchanged (97). In patients with low clinical probability, the posttest probability of having DVT after a negative D-dimer test result is less than 1% (48). This is true whether using a moderate- or high-sensitivity D-dimer assay (48). D-dimers are degradation products of cross-linked fibrin generated during fibrinolysis. However, D-dimer is not a single entity in plasma but, rather, a mixture of heterogeneous fibrin degradation products. Different assays measure different types of D-dimer; consequently, test results are reported as μg/mL D-dimer units (D-DU), μg/mL fibrinogen equivalent units (FEU), or ng/mL. No single cut-off value for all assays exists, and attempts to standardize D-dimer testing have failed (98). Hence, thresholds and interpretation of test results are supplied by the manufacturer and vary from assay to assay. A negative D-dimer test result using laboratory-based assessments and newer point-of-care tests appear to be equally effective in ruling out DVT (50).

A venous duplex ultrasound study should be performed in patients with a moderate to high pretest probability of DVT (51,94–96). These scans should also be obtained in patients with low pretest probability and a positive D-dimer test result (51,94–96). There are 2 types of studies currently recommended:

1. Serial proximal venous system ultrasonography
2. Single scanning of the entire symptomatic extremity

The advantages of serial scanning are its simplicity, reproducibility, and broad availability. If a proximal venous scan is initially negative for DVT, a D-dimer level or repeat proximal venous scan should be obtained 7 to 10 days later to ensure that no proximal propagation of a distal DVT has occurred (13). It is important to recognize that bilateral lower extremity scanning is not required. Furthermore, obtaining routine venous ultrasound duplex scans in asymptomatic postoperative patients is not recommended.

Single scanning of the entire symptomatic extremity (also called whole leg ultrasound) was recognized as the preferred method by the consensus panel. The main advantages of whole leg ultrasound are that it obviates the need for a return patient visit and repeat testing, and it provides more accurate assessment of distal DVT that could lead to Pts if left untreated (8,9,99). Concerns with the use of whole leg ultrasound include the amount of time required, regional availability, and the cost of performing the study. A recent systematic review and meta-analysis including more than 4,700 patients concluded that a single whole leg ultrasound is safe and accurate, as a negative scan was associated with a low risk for VTED during 3 month follow-up (pooled incidence rate = 0.57%, 95% CI 0.25% to 0.89%) (47). However, this study cannot be performed with lower extremity immobilization in place and may be less reliable in patients with severe edema, severe obesity, acute infection, or active cancer (100).

### Conclusion

Routine chemical prophylaxis is not warranted in foot/ankle surgery or injuries requiring immobilization. Rather foot and ankle surgeons should attempt to stratify patients and develop a prophylaxis plan for those at high risk of VTED. Risk factors may be patient-specific, related to the treatment course, and/or related to the surgery or injury itself. Primary risk factors include a personal history of VTED, active or recent cancer, hypercoagulability, and prolonged lower extremity immobilization. Secondary risk factors include obesity, advanced age, OCP/HRT use, family history of VTED, varicose veins, higher injury severity score, diabetes mellitus or more than one comorbidity, non-weightbearing status, hospitalization, bed rest, general anesthesia, and some hindfoot and lower leg surgeries and injuries. Multimodal VTED prophylaxis strategies should focus on addressing modifiable risk factors, use of mechanical prophylaxis, early mobilization, and careful consideration of the use of chemical prophylaxis. The final decision regarding use and method(s) of prophylaxis adopted should be agreed upon by the physician and patient after a discussion of the potential benefits and harms as they relate to the individual. This should preferably take place during the preoperative visit or in the immediate post-injury setting, and the use and/or method(s) chosen may need to be revisited during the course of care if the patient’s risk level changes. Prompt recognition of DVT in the outpatient setting is important, as the consequences of misdiagnosis can be serious and potentially fatal. Patients with a suspected DVT should undergo a work-up with either a D-dimer test or duplex venous ultrasound of the symptomatic leg, depending on their pretest probability for the disease. The latter can be determined using a validated clinical decision-making tool (e.g., Well’s criteria).

### Supplementary Material

Supplementary material associated with this article can be found in the online version at [www.jfas.org](http://www.jfas.org). http://dx.doi.org/10.1053/j.jfas.2015.02.022.