

# Emergency Department Management of Suspected Calf-Vein Deep Venous Thrombosis: A Diagnostic Algorithm

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Section Editor: Mark I. Langdorf, MD, MHPE

Submission history: Submitted February 2, 2016; Revision received March 31, 2016; Accepted May 3, 2016

Electronically published June 28, 2016

Full text available through open access at [http://escholarship.org/uc/uciem\\_westjem](http://escholarship.org/uc/uciem_westjem)

DOI: 10.5811/westjem.2016.5.29951

**Introduction:** Unilateral leg swelling with suspicion of deep venous thrombosis (DVT) is a common emergency department (ED) presentation. Proximal DVT (thrombus in the popliteal or femoral veins) can usually be diagnosed and treated at the initial ED encounter. When proximal DVT has been ruled out, isolated calf-vein deep venous thrombosis (IC-DVT) often remains a consideration. The current standard for the diagnosis of IC-DVT is whole-leg vascular duplex ultrasonography (WLUS), a test that is unavailable in many hospitals outside normal business hours. When WLUS is not available from the ED, recommendations for managing suspected IC-DVT vary. The objectives of the study is to use current evidence and recommendations to (1) propose a diagnostic algorithm for IC-DVT when definitive testing (WLUS) is unavailable; and (2) summarize the controversy surrounding IC-DVT treatment.

**Discussion:** The Figure combines D-dimer testing with serial CUS or a single deferred FLUS for the diagnosis of IC-DVT. Such an algorithm has the potential to safely direct the management of suspected IC-DVT when definitive testing is unavailable. Whether or not to treat diagnosed IC-DVT remains widely debated and awaiting further evidence.

**Conclusion:** When IC-DVT is not ruled out in the ED, the suggested algorithm, although not prospectively validated by a controlled study, offers an approach to diagnosis that is consistent with current data and recommendations. When IC-DVT is diagnosed, current references suggest that a decision between anticoagulation and continued follow-up outpatient testing can be based on shared decision-making. The risks of proximal progression and life-threatening embolization should be balanced against the generally more benign natural history of such thrombi, and an individual patient's risk factors for both thrombus propagation and complications of anticoagulation. [West J Emerg Med. 2016;17(4)384-390.]

## INTRODUCTION

### Clinical Scenario

Our interest in this topic was prompted by two emergency department (ED) visits by an 84-year-old man. Initially, he presented with right calf swelling 10 days after shoulder surgery. Bedside compression ultrasound (CUS) was negative for proximal deep venous thrombosis (DVT), and a D-dimer was elevated at 3.3µg/mL. Right calf DVT was strongly suspected and he was treated with therapeutic enoxaparin. Whole leg ultrasound (WLUS) 36 hours later diagnosed chronic DVT in the right gastrocnemius veins. Therapeutic enoxaparin was continued by his physicians. He returned to our

ED six days after his initial visit with right shoulder pain and an 18cmx7cm chest wall hematoma with evidence of active bleeding. Inpatient management consisted of protamine reversal of his enoxaparin and transfusion of blood and platelets.

### Background

In emergency patients, acute unilateral leg pain and/or swelling are common complaints, often prompting a search for DVT. Proximal DVT (with its risk for pulmonary embolism [PE]) is commonly ruled in or out during the initial ED encounter.<sup>1,2</sup> As in our patient, when proximal DVT is eliminated, isolated calf deep vein thrombosis (IC-

DVT) often remains in the differential diagnosis. Whole-leg duplex ultrasonography (WLUS), the current standard for an affirmative diagnosis of IC-DVT, is unavailable after-hours in many EDs.<sup>3,4</sup> The purpose of this article is to suggest an algorithm for the evaluation of patients with suspected IC-DVT when WLUS is unavailable. Treatment controversies surrounding this entity are described.

## DISCUSSION

### The Nature of the Problem

No one would deny the frequency and importance of DVT, which affects around one in 1,000 persons per year.<sup>5</sup> Emergency physicians appropriately have a high degree of concern for this condition. We look for it frequently, and DVT is found in 10-25% of patients in whom it is suspected.<sup>6</sup> We seek to diagnose proximal DVT to prevent PE and the postthrombotic syndrome. When proximal DVT is ruled out, distal thrombus must often still be considered. We pursue the diagnosis of IC-DVT out of concern for the progression of these distal thrombi to proximal DVT and PE. In community practice, isolated calf DVT was diagnosed in 11% of 1,495 patients in whom it was suspected.<sup>7</sup> When all patients undergo WLUS, IC-DVT is even more frequently found, representing about 50% of diagnosed DVTs.<sup>8</sup> The majority of distal thrombi are non-obstructive and asymptomatic and long-term outcomes are similar in patients diagnosed using either proximal or whole-leg imaging.<sup>9,10</sup>

### IC-DVT: Risk of Thrombus Propagation, Mortality, and Pulmonary Embolism

All DVT is assumed to start in the calf veins.<sup>11</sup> Untreated, symptomatic IC-DVT progresses to involve the popliteal or femoral veins  $\leq 16\%$  of the time.<sup>1,12-14</sup> Such propagation has not been documented after two weeks.<sup>13,15-17</sup> Risk factors promoting propagation include a history of cancer, inpatient status, positive D-dimer, extensive thrombus or proximity to proximal veins, absence of reversible provoking factors for DVT, history of trauma and history of prior venous thromboembolism (VTE).<sup>13</sup>

Calf vein DVT, with or without treatment, has a mortality of  $\leq 1\%$ .<sup>1</sup> When the search for DVT begins after a diagnosis of PE is made, 7-11% of patients with suspected symptomatic PE will have IC-DVT.<sup>18</sup> If tested, 13% of patients with proven IC-DVT will have evidence of "silent" PE.<sup>19</sup> The controversy surrounding the significance of diagnosing and treating small or minimally symptomatic PEs is under active discussion, and is not covered here.<sup>20,21</sup>

### How Should the Diagnosis of Suspected IC-DVT Be Approached?

When available, WLUS rules out IC-DVT with a subsequent composite VTE complication rate of  $\leq 1\%$ .<sup>5,8,10,22-24</sup> In the absence of WLUS, commonly available diagnostic modalities are bedside (or radiology department) proximal

compression ultrasonography, clinical probability assessments, and D-dimer testing.

### The Role of D-dimer Testing, Pretest Clinical Probability, and Compression Ultrasonography

**D-dimer and Clinical Probability:** For both DVT in general, and isolated calf DVT specifically, the negative predictive value (NPV) of a D-dimer in low-risk patients (Wells score of zero or less) is  $\geq 99\%$ .<sup>6,25</sup> The 2012 American College of Chest Physicians (ACCP) Clinical Practice Guidelines for Antithrombotic Therapy and Prevention of Thrombosis endorses a strategy for diagnosing DVT combining D-dimer testing with pretest probability assessment using the Wells score.<sup>5</sup> In patients with a negative D-dimer and a low pretest probability of first lower extremity DVT, Wells et al. 2003 and 2006 and the ACCP 2012 guidelines support no further testing.<sup>5,6,26</sup> With an elevated D-dimer, ACCP recommendations are for proximal compression ultrasound.

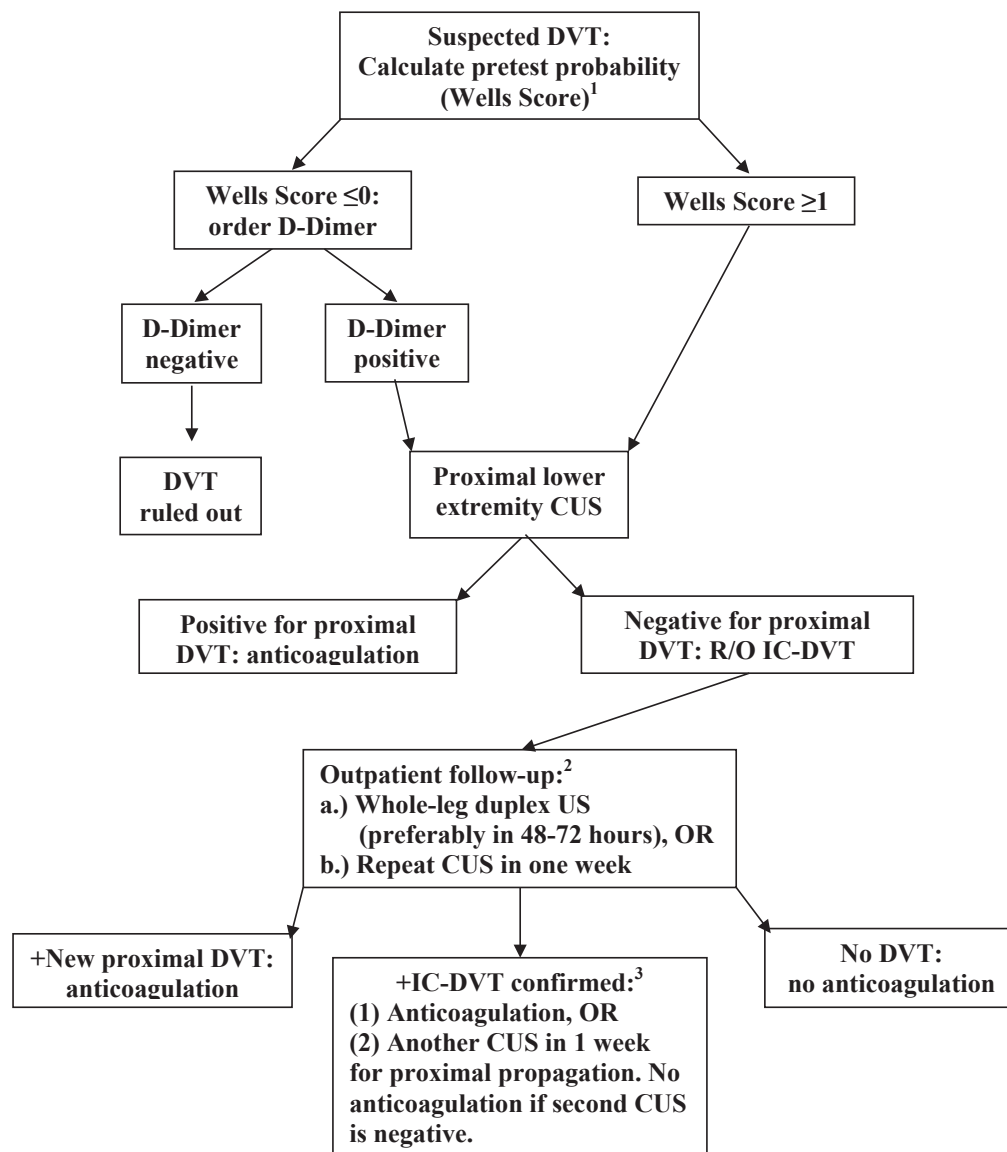
**Compression Ultrasound (CUS):** In the absence of WLUS, the presence of a positive D-dimer or a moderate or high clinical probability Wells score should be followed by compression ultrasonography in the ED to rule out proximal DVT. A positive CUS would identify the need for therapeutic anticoagulation. The significant numbers of emergency physicians trained in bedside CUS make that modality increasingly more accessible and often more available than radiology studies, particularly outside normal business hours. Multiple studies have demonstrated that proximal DVT can reliably be diagnosed or excluded in the ED with bedside proximal CUS with sensitivities of 95-99%.<sup>27-30</sup> Formal radiology CUS remains an option when available. The additional value of initially combining both CUS and a D-dimer has yet to be specifically studied. However, when both tests are done and negative, the combination effectively excludes any clinically significant DVT ( $\geq 99\%$  NPV).<sup>10,26,31-34</sup> The combination has been recommended in patients with high clinical pretest probability.<sup>5</sup>

## RECOMMENDATIONS

### Diagnosis of IC-DVT in the Setting of Positive D-dimer and Negative CUS for Proximal DVT

When the D-dimer is positive and CUS is negative, WLUS is the definitive diagnostic test and the procedure of choice. When WLUS is not immediately available, the ACCP recommends two strategies presented in the Figure: either direct imaging of the calf veins with a short-term definitive whole-leg ultrasound, or a repeat proximal CUS in a week to assess for proximal progression.<sup>5</sup> The 1-week repeat CUS has been found to be both equivalent to a single WLUS in ruling out IC-DVT likely to progress, and safe (0-1.8% VTE at 3-6 months).<sup>10,23,31-36</sup>

For the many emergency patients for whom outpatient testing and follow up cannot be reliably arranged, the ability to rule out proximal propagation of suspected IC-DVT with



**Figure.** Proposed emergency department DVT evaluation algorithm when full-leg vascular duplex ultrasonography is unavailable. ACCP, American College of Chest Physicians; CUS, compression ultrasound; DVT, deep venous thrombosis; IC-DVT, isolated calf deep venous thrombosis; R/O, rule out; US, ultrasound.

1. The pretest probability of DVT is most frequently assessed with the clinical model developed by Wells, et al.[6] One point is added for each of the following positive findings: (i) active cancer (treatment ongoing or within the previous 6 months, or palliative); (ii) paralysis, paresis or recent plaster immobilization of the lower extremities; (iii) recently bedridden for 3 days or more, or major surgery within the previous 12 weeks requiring general or regional anesthesia; (iv) localized tenderness along the distribution of the deep venous system; (v) entire leg swelling; (vi) calf swelling at least 3 cm larger than that on the asymptomatic leg (measured 10 cm below the tibial tuberosity); (vii) pitting edema confined to the symptomatic leg; (viii) collateral superficial veins (nonvaricose); and (ix) previously documented DVT. Two points are subtracted from the total if an alternative diagnosis is at least as likely as DVT. Based on this checklist the clinical probability of DVT is assessed as low if the score is  $\leq 0$ , moderate (a score of 1 or 2), or high (a score of  $\geq 3$ ). The ability of a negative D-dimer to rule out DVT at a given pretest clinical probability (Well's score) is dependent upon the sensitivity of the specific assay used. When a negative high-sensitivity D-dimer is combined with a low ( $\leq 0$ ) or moderate ( $\leq 2$ ) Well's score, the negative predictive value for DVT is 99%. This is reflected in the algorithm. Wells, et al. (2006) conclude that with moderate sensitivity D-dimer tests "the negative LRs are not sufficiently low to exclude DVT without ultrasound among patients with moderate and high pretest probability estimates" (Well's score  $\geq 1$ ). [6]

2. The practice of providing a bridge of empiric anticoagulation between imaging studies is not supported.[10, 23, 31-34, 36]

3. Per ACCP and others, the decision to anti-coagulate confirmed IC-DVT (versus conservative therapy) benefits from a thorough risk/benefit analysis and shared decision-making. Risk factors for extension of confirmed IC-DVT include positive D-dimer, severe symptoms, thrombosis that is extensive or close to the proximal veins, absence of reversible provoking factors for DVT, active cancer, a history of venous thromboembolism (VTE), and inpatient status. Those at higher risk for bleeding complications from anticoagulation may be better served by continued surveillance with compression ultrasonography alone (Keaton, et al.; Table 11).[13,14] The patient's primary provider and/or consultants should be involved in the decision-making whenever possible, with every effort to assure close follow up.

repeat ED bedside compression ultrasound, makes return to the ED for such testing an option.

### **Bridging Anticoagulation**

When proximal DVT has been ruled out in the ED and suspected IC-DVT is being investigated with planned short-term deferred WLUS or repeat proximal CUS, the practice of providing a bridge of empiric anticoagulation between imaging studies is not supported.<sup>4,10,23,31-34,36</sup>

### **Treatment of Confirmed IC-DVT - Selective Anticoagulation is Controversial**

We present an algorithm for the diagnosis of IC-DVT when definitive WLUS is not immediately available. Treatment for IC-DVT is controversial, and will only be briefly reviewed here.<sup>1,9,14,36-40</sup> Previous ACCP guidelines, current European guidelines and commonly used references (UpToDate) recommend treating IC-DVT with at least three months of anticoagulation.<sup>41,42,43</sup> The latest ACCP guidelines include a more selective approach.<sup>13</sup> The controversy is best exemplified by a survey of faculty physicians at a major U.S. medical center. Half of respondents would “routinely use anticoagulation to treat venous thrombosis below the knee” and half would not.<sup>44</sup> There is a near-universal call for large randomized trials to address the question. One such trial is underway ([www.ClinicalTrials.gov](http://www.ClinicalTrials.gov)).<sup>45</sup> In the absence of new and definitive data, and as suggested by the ACCP, recommendations to base treatment decisions on risk/benefit analysis and shared decision-making are becoming more common.<sup>1,12,13</sup>

The controversy over treatment largely derives from an increase in the frequency of diagnosis of IC-DVT, coupled with conclusions that distal DVT is less concerning than proximal. When WLUS is used instead of CUS, the reported prevalence of distal DVT rises to half of all lower extremity DVTs.<sup>36</sup> However, risk factors associated with distal DVTs are more commonly transient and reversible, and mortality and recurrence rates are less.<sup>18,46,47</sup> Those in favor of observation rather than treatment for IC-DVT note that untreated patients with negative proximal CUS (many of whom would likely have IC-DVT if looked for) demonstrate an acceptable outcome profile without treatment.<sup>14,36</sup> Treating them all exposes patients to unnecessary bleeding complications.<sup>18,23,36,48</sup> Our patient is an example.

### **Selective Treatment of Confirmed IC-DVT - Shared Decision-Making**

The ACCP evidence-based clinical practice guidelines (currently in their 10th edition, spanning 30 years) provide a solid starting point for clinical decision-making.<sup>5,13,49,50</sup> The most recent edition offers two options for confirmed IC-DVT: (1) therapeutic anticoagulation or (2) weekly surveillance with compression ultrasonography for two weeks to monitor for proximal thrombus propagation.<sup>13</sup> They suggest that

those with severe symptoms or with risk factors for proximal extension should receive anticoagulation. Patients at risk for anticoagulation-associated major bleeding (see Table 11, Kearon et al., 2016) may be better served by surveillance. For those at lower risk for both propagation and hemorrhage there may be room to consider a more selective approach using shared decision-making.<sup>13,14,51</sup> Discussions should be well documented and focus on the patient’s valuation of, and ability to comply with, serial surveillance for clot propagation versus their tolerance for the risks of bleeding associated with prevention. Given the controversy over IC-DVT treatment, the patient’s primary provider and/or consultants should be involved in the decision-making whenever possible, with every effort to assure close follow up. There is a lack of data comparing management strategies for IC-DVT in patients with varying levels of these conflicting risks.

### **Therapeutic Adjuncts**

The role of compression stockings for comfort and for the prevention postthrombotic syndrome (PTS) has not been studied for IC-DVT. For proximal DVT, adverse events from stockings are rare and minor, but their value for preventing PTS is “in doubt.”<sup>52-54</sup> No recommendations could be found for the role of aspirin in the treatment of IC-DVT.

### **LIMITATIONS**

Data on the prevalence of DVT overall and the subset of IC-DVT vary significantly. While the number of reports is considerable, many are derived from small underpowered observational cohort studies, subsequently folded into meta-analyses. Explanations for variability include the size and heterogeneity of the patient population (inpatient, outpatient, community, post-surgical, trauma, presence or absence of symptoms), the reason for testing (suspected or confirmed PE, versus DVT), and the diagnostic imaging used. Most series did not image the entire leg.

The algorithm suggested is based on the latest evidence and practice guidelines. Like so much of the literature on this topic, it would benefit from prospective controlled evaluation.

Any strategy involving compliance with return visits (surveillance) loses some patients to follow up.<sup>18,55</sup> During the period covered by this discussion, D-dimer assays evolved and the Wells clinical prediction rules were modified.<sup>6,26,56</sup> Current recommendations are predicated on the use of high-sensitivity D-dimer assays.<sup>5,57</sup> Multiple such assays are in use.<sup>58</sup> Both the Wells criteria and D-dimer assays have greater sensitivity for proximal than isolated distal DVT.<sup>25,59-61</sup>

Leg pain and swelling are among the common ED complaints that trigger a search for serious conditions requiring urgent intervention. Yet <25% will have DVT. Even applying clinical decision rules and diagnostic tests with 99% sensitivity, physicians will see false negatives with serious consequences, as seen in multiple case reports available in the literature.<sup>62-64</sup> Clinical judgment, “high index of suspicion,”

patient education, comprehensive discharge instructions, and close follow up remain tools we need to routinely apply.

Muscular calf vein thrombosis: Roughly half of calf vein thromboses are isolated to the veins of the soleus and gastrocnemius muscles.<sup>65</sup> Although these are most often considered “deep” veins, thrombosis confined to the muscular veins has a “lower risk of extension than thrombosis that involves the axial (i.e., true deep; peroneal, tibial) veins.”<sup>13</sup> Although subject to similar variability in opinion as DVT treatment in general, anticoagulation of calf muscle thrombosis is less commonly favored.<sup>15,66,67</sup>

## CONCLUSION

Unilateral leg pain/swelling is a common ED complaint. The diagnosis of isolated calf vein DVT is particularly challenging when the definitive diagnostic study, whole-leg ultrasound, is unavailable. An ED diagnostic algorithm is presented for this situation, based on the most recent recommendations of the American College of Chest Physicians. It is important to remember that this algorithm is based on critical appraisal of the current literature and will require prospectively controlled studies before it can be recommended for widespread implementation. Treatment is controversial: universal versus selective anticoagulation. The risks of proximal progression and life-threatening embolization should be considered along with the generally more benign natural history of distal clots and an individual patient’s risk factors for both clot propagation and the complications of therapy.

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