



## Should we diagnose and treat distal deep vein thrombosis?

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Ultrasound series report that isolated distal deep vein thrombosis (DVT), also known as calf DVT, represents up to 50% of all lower-limb DVTs and, therefore, is a frequent medical condition. Unlike proximal DVT and pulmonary embolism, which have been studied extensively and for which management is well standardized, much less is known about the optimal management of isolated calf DVT. Recent data arising from registries and nonrandomized studies have suggested that most distal DVTs do not extend to the proximal veins and have an uneventful follow-up when left untreated. These data had some impact on the international recommendations that recently stated that ultrasound surveillance instead of systematic therapeutic anticoagulation might be an option for selected low-risk patients. However, robust data from randomized studies are scarce. Only 5 randomized trials assessing the need for anticoagulation for calf DVT have been published. Many of these trials had an open-label design and were affected by methodological limitations. The only randomized placebo-controlled trial included low-risk patients (outpatients without cancer or previous venous thromboembolism [VTE]) and was hampered by limited statistical power. Nevertheless, data from this trial confirmed that the use of therapeutic anticoagulation in low-risk patients with symptomatic calf DVT is not superior to placebo in reducing VTE but is associated with a significantly higher risk of bleeding. Further randomized studies are needed to define the best therapy for high-risk patients (inpatients, patients with active cancer, or patients with previous VTE) and the optimal dose and duration of treatment.

### Learning Objectives

- Limited data support an evidence-based treatment of symptomatic distal deep vein thrombosis
- Ultrasound surveillance without therapeutic anticoagulation is a management option in low-risk (ie, no active cancer and no previous venous thromboembolism) with symptomatic distal deep vein thrombosis

### Introduction

Isolated distal deep vein thrombosis (DVT), that is, infrapopliteal DVT without extension to proximal veins (popliteal vein or above) or pulmonary embolism (PE), also known as calf DVT, is frequent and represents 30% to 50% of all lower-limb DVTs diagnosed on ultrasound series.<sup>1-3</sup> Unlike for proximal DVT and PE, which have been extensively studied and for which management is well standardized and the subject of high-level evidence and recommendations, much less is known about the optimal management of isolated distal DVT.<sup>4</sup>

The rate of extension to the proximal veins and the rate of PE associated with distal DVT are highly variable from one study to another. As a result, significant variation exists in diagnostic and therapeutic practices across centers.<sup>1,5-8</sup> In some centers, both the proximal veins and the calf veins are imaged in all patients with suspected DVT, and patients diagnosed with isolated calf DVT are

treated with anticoagulant therapy.<sup>9</sup> Other centers rely on serial imaging of the proximal veins only and, thus, do not diagnose or treat calf DVT.<sup>10</sup> In the latter strategy, in case of a negative proximal ultrasound, the test often is repeated 1 week later to rule out extension of a calf DVT to the proximal veins. Comparisons between these 2 diagnostic strategies have shown that the proportion of patients diagnosed with DVT and thus treated with anticoagulants is higher when using whole-leg imaging compared with serial proximal imaging. Nevertheless, diagnosing and treating distal DVT has not been associated with better overall safety for patients. Indeed, the 3-month venous thromboembolism (VTE) risk was equivalent in patients left without treatment on the basis of either strategy.<sup>11,12</sup> These results thus question the need to systematically diagnose and treat all calf DVTs with anticoagulants, particularly in patients free of any of the major strongly identified predictors of DVT extension and recurrence (inpatients, patients with a history of a previous VTE, or patients with cancer) who represent the majority of those with calf DVT.<sup>4,13-15</sup>

### Epidemiology and natural history of distal DVT

In inpatient studies, 80% of all diagnosed DVTs are proximal, and 20% are calf.<sup>16-18</sup> However, some studies in outpatients diagnosed with DVT by compression ultrasound (CUS) report a proportion of calf DVT as high as 60% to 70%, underlining the potential relevance of the problem in everyday clinical practice.<sup>19,20</sup>

The natural history of DVT seems to be, in the majority of cases, the development of a thrombus in the distal veins of the calf that extends proximally—the so-called ascending pattern of thrombus extension.<sup>18</sup>

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Whereas the embolic potential of proximal DVT is unanimously recognized, distal clots appear to have a much lower embolic potential, although data remain limited.<sup>21</sup> Therefore, the rate of extension of distal DVT to the proximal veins and the rate of PE are crucial issues because they largely determine the clinical significance of distal DVT in terms of patient outcomes and, hence, in terms of the need for treatment.

*Assessing the risk of proximal extension without treatment.* Performing a thorough estimation of the risk of extension of distal DVT to proximal DVT and/or PE remains difficult. Indeed, the rate of extension among studies is highly variable because of high heterogeneity in patient populations, clinical settings, and diagnostic strategies.<sup>2,22</sup> Comparison between studies also is limited by disparity in treatment regimens as well as major differences in the follow-up and definition of outcomes (symptomatic extension vs extension diagnosed on systematic testing).

An interesting approach to assessing the rate of extension of distal DVT to the proximal veins is the use of data arising from diagnostic studies that are based on serial proximal CUS (described in detail in “Various lower-limb venous ultrasound strategies for suspected DVT”). These studies show a low rate of proximal DVT (1%-5.7%; not shown in Table 1) detected by the repeated proximal CUS in patients left untreated after a first negative CUS limited to the proximal veins (Table 1). Of note, these studies mainly include outpatients with suspected DVT, so the rather low reported rates of extension to proximal veins could reflect the natural history of untreated calf DVT in low-risk patients.

*Comparison of outcomes between treated and untreated patients.* Variations in study design and target populations are too large to allow a clinically relevant pooled estimate to compare the proportion of treated and untreated patients with distal DVT who experience an extension to proximal DVT. Nevertheless, a systematic review published in 2006 reported an estimated rate of extension of 10% (95% CI, 7%-12%) in untreated patients and of 4% (95% CI, 3%-6%) in treated patients.<sup>2</sup>

A recent systematic review that included prospective cohort studies and some of the most recent randomized studies reported an overall proximal extension rate that varied between 0% and 35%, which corresponds to a mean extension rate of 9%.<sup>22</sup> Although the true significance of a mean value in view of the large heterogeneity of studies can be debated, it helps to give a rough idea of the potential range of the extension rate. The reported rate of PE ranged from 0% to 5.8% with a mean rate of 1.4%. None of the available studies found that anticoagulant treatment was associated with a reduction in adverse outcomes. In terms of bleeding, the major bleeding rate (excluding an older study that showed a high major bleeding rate of 7%) was 0% to 2.1% in patients treated with anticoagulants, whereas no major bleeding was reported in patients who did not receive anticoagulant treatment. All these elements highlight the uncertainty about the natural history of distal DVT, its clinical significance, and the need for and modality and duration of treatment. In view of the uncertainty about the necessity to treat distal DVT, the question of the necessity to diagnose distal DVT can be raised. Because the diagnostic management of distal DVT varies as widely as its therapeutic management among centers, this issue is discussed in detail next.

#### *Various lower-limb venous ultrasound strategies for suspected DVT*

Distal or calf DVT involves the infrapopliteal veins, which are the posterior tibial veins, peroneal veins, anterior tibial veins, and muscular calf veins (soleus or gastrocnemius veins). The sensitivity

**Table 1. Performances and safety of proximal compression ultrasonography for diagnosing DVT in outcome management studies**

Reference	Patients, No.	Prevalence of DVT, %	Three-month thromboembolic risk, % (95% CI)*
Birdwell et al <sup>27</sup>	405	16	0.6 (0.1-2.1)
Wells et al <sup>10</sup>	1702	24	0.7 (0.3-1.2)
Bernardi et al <sup>28</sup>	946	28	0.4 (0-0.9)
Wells et al <sup>30</sup>	593	16	0.6 (0.1-1.8)
Kraaijenhagen et al <sup>29</sup>	1756	22	0.7 (0.3-1.6)
Pooled estimate	5876	23	0.5 (0.4-0.9)

Distal DVTs were not searched for in these studies.

\*During 3-mo follow-up in patients left untreated after normal proximal CUS.

and specificity of CUS for proximal DVT are high (97% and 98%, respectively),<sup>23</sup> and the necessity for treating proximal DVT with anticoagulants is widely accepted.<sup>24</sup> On the other hand, the sensitivity and specificity of CUS for distal DVT are lower.<sup>16,23</sup> A meta-analysis by Kearon et al<sup>23</sup> reported a sensitivity of 50% to 75% and specificity of 90% to 95%. Another more recent meta-analysis published in 2005 suggested similar values for ultrasound accuracy for calf thrombosis.<sup>25</sup> Some studies by highly skilled ultrasonographers who used the best ultrasound machines reported much higher accuracy.<sup>26</sup> The improvement in ultrasound technology and increased experience in the field have led to a reliable diagnosis of distal DVT in experienced hands when the most reliable diagnostic criterion is used: the lack of compressibility of a venous segment.

*Serial proximal CUS in outcome studies.* The limited performance of distal venous examination reported in some studies may explain why many centers use only proximal CUS (ie, limited to the popliteal and suprapopliteal veins). Because such protocols do not search for distal DVT, which if present, could potentially extend to the proximal veins with a significant risk of PE, the standard diagnostic approach consists of performing a second CUS limited to the proximal veins at day 7—the so-called serial proximal CUS strategy. Patients with a proximal DVT on the initial CUS are treated with anticoagulants. When the initial examination is negative, patients are not given anticoagulants, and a second proximal CUS is repeated 1 week later to detect the possible extension of distal DVT. Patients with a second normal CUS are considered as definitely not having a DVT and are not anticoagulated.

Many well-designed prospective outcome studies have shown the safety of proximal CUS integrated in diagnostic strategies (Table 1). The 5 studies used CUS limited to the proximal veins.<sup>10,27-30</sup> The pooled estimate of the 3-month thromboembolic risk of these prospective management studies was 0.5% (95% CI, 0.4%-0.9%). There was no significant difference in the 3-month thromboembolic risk among these studies. If one considers each study individually, the 3-month thromboembolic risk in patients with a negative proximal CUS is low because it was <1%.<sup>10,27-30</sup> Even if serial proximal CUS is safe, its main limitation is the need for a second ultrasound examination, which is cumbersome and costly and has a very low yield, because it reveals a proximal DVT in only 1% to 5.7% of patients.

*Single complete (proximal and distal) CUS in suspected DVT.* Seven prospective outcome studies that used a single complete (ie, proximal, distal) CUS have been published (Table 2).<sup>11,26,31-35</sup> Patients were treated if CUS showed a proximal or distal DVT and were

**Table 2. Performances and safety of a single proximal and distal (whole-leg) CUS for diagnosing DVT in outcome management studies**

Reference	Patients, No.	Prevalence of all DVT, No. (%)	Distribution of DVT level, No. (%)		Three-month thromboembolic risk, % (95% CI)*
			Proximal	Distal	
Elias et al <sup>26</sup>	623	204 (33)	112 (55)	92 (45)	0.5 (0.1-1.8)
Schellong et al <sup>31</sup>	1 646	275 (17)	121 (44)	154 (56)	0.3 (0.1-0.8)
Stevens et al <sup>32</sup>	445	61 (14)	42 (69)	19 (31)	0.8 (0.2-2.3)
Subramaniam et al <sup>33</sup>	526	113 (22)	49 (43)	64 (57)	0.2 (0.01-1.3)
Bernardi et al <sup>11</sup>	1 053	278 (26)	213 (76)	65 (24)	1.2 (0.5-2.2)
Sevestre et al <sup>35</sup>	3 871	1 023 (26)	454 (44)	569 (56)	0.6 (0.3-1.2)
Sevestre et al <sup>34</sup>	1 926	395 (21)	155 (39)	240 (61)	0.6 (0.1-1.7)
Pooled estimate	10 090	2 349 (23)	1 146(49)	1 203 (51)	0.6 (0.3-0.9)

\*During 3-mo follow-up in patients left untreated after a normal complete (proximal and distal) CUS.

left untreated if proximal and distal veins were normal without further testing. These studies confirmed the safety of a single complete CUS, with a pooled estimate of the 3-month thromboembolic risk of 0.6% (95% CI, 0.3%-0.9%).<sup>9</sup>

However, despite their diagnostic safety, these studies point to some important problems. First, such an approach is costly and time consuming because complete CUS is proposed for all patients with suspected DVT. Indeed, in outpatients with clinically suspected DVT, a normal enzyme-linked immunosorbent assay D-dimer test allows the withholding of anticoagulation without further testing in approximately one third of outpatients at a much lesser expense and with a similar safety.<sup>36</sup> Second, the pooled estimate of the 3-month VTE risk of these studies is similar to that computed for studies that use only proximal CUS (Tables 1 and 2). This means that detecting calf DVT actually may be deleterious: It does not reduce the 3-month VTE risk and entails a risk of unnecessary anticoagulant treatment in patients who would have fared well without it. Moreover, because of the limitations in the diagnostic performance of CUS at the calf level, some of the positive findings might even be false positives, rendering the potentially unnecessary exposure to bleeding risk associated with anticoagulation even more unacceptable. To give an idea of the extent of this issue, a pooled analysis of studies of complete CUS has shown that among 10 090 included patients, 1203 of 2343 diagnosed DVTs (51%) were distal (Table 2).

*Serial proximal vs single complete (proximal and distal) CUS in suspected DVT.* The next logical step is to perform a direct comparison between serial proximal CUS and single complete CUS diagnostic strategies for DVT, which was performed in 3 studies with similar results.<sup>11,12,37</sup> Therefore, only the most robust study in terms of methodology will be discussed here.<sup>11</sup> In this prospective, randomized, multicenter trial, a strategy that included serial 2-point (femoral and popliteal) proximal CUS associated with D-dimer testing was compared with a single whole-leg CUS strategy in >2000 outpatients with a clinical suspicion of DVT. In the proximal CUS arm, patients with a normal 2-point CUS underwent qualitative D-dimer testing (SimpliRED, Agen Biomedical, Melbourne, QLD, Australia). Patients with negative D-dimer results were spared further investigations and not treated with anticoagulants. Only patients with abnormal D-dimer levels underwent the repeat CUS at 1 week. Both strategies reported a similar 3-month rate of VTE (0.9% [95% CI, 0.3%-1.8%] for the 2-point proximal CUS and D-dimer arm vs 1.2% [95% CI, 0.5%-2.2%] for the complete single CUS arm). The safety of both strategies, therefore, was similar. Of note, 23% (65 of 278) of patients with confirmed DVT in

the complete single CUS arm were treated with an anticoagulant for a distal DVT without decreasing the 3-month VTE risk.

To decrease the number of patients undergoing a distal vein examination, a new diagnostic strategy was evaluated in a prospective outcome study.<sup>38</sup> All patients with suspected DVT had a clinical probability assessment. Patients with suspected DVT had a whole-leg CUS (ie, proximal, distal) only in the case of both a likely clinical probability and a positive D-dimer measurement. Patients with an unlikely probability and negative D-dimer result did not undergo CUS and were left untreated. All other patients with a positive D-dimer result had a single proximal CUS. The overall prevalence of DVT was 18% in the whole cohort. Among all confirmed DVTs, 39% were isolated distal DVTs, which is lower than the pooled estimate of 51% in studies of complete CUS for all patients (Table 2). Despite a lower rate of detection of distal DVT, this strategy was revealed to be safe, with a 3-month VTE risk of 0.9% (95% CI, 0.44%-1.70%).

#### *D-dimers in the diagnosis of calf DVT*

The safety and cost-effectiveness of D-dimer measurement in the diagnosis of patients with suspected DVT has been extensively studied. D-dimer measurement has been proven to be highly sensitive but not specific for the presence of VTE and to be associated with a high negative predictive value for DVT in various patient populations.<sup>36,39,40</sup>

D-dimer seems to have a lower sensitivity and negative predictive value for calf DVT than for proximal DVT. For example, Jennersjö et al<sup>41</sup> reported that as many as 35% of patients with calf DVT may have normal D-dimer levels, suggesting a limited sensitivity of the test to rule out distal DVT. However, other studies have reported much higher sensitivities,<sup>42,43</sup> rendering a robust evaluation of D-dimer sensitivity for distal DVT quite difficult. Nevertheless, a meta-analysis showed that all D-dimer assays had a higher sensitivity for proximal than for distal DVT (98% vs 86% for enzyme-linked immunosorbent assay, 94% vs 79% for latex agglutination, 84% vs 64% for whole-blood agglutination).<sup>44</sup> Altogether, these data suggest that D-dimer measurements are less sensitive at the distal than at the proximal level and that some patients may have a distal DVT and D-dimer levels below the usual cutoff value of 500 ng/mL. However, one should keep in mind that in terms of patient outcomes, many prospective outcome studies in several thousands of patients have shown that patients with suspected PE or DVT have a very-low 3-month VTE rate (<1%) when left untreated on the basis of a negative D-dimer test result.<sup>45</sup> Therefore, we still believe that the

**Table 3. Major efficacy and safety outcomes at day 42 in the CACTUS trial**

	Therapeutic nadroparin (n = 122), No. (%)	Placebo (n = 130), No. (%)	Absolute risk difference, % (95% CI)	P
Primary outcome by day 42	4 (3.3)	7 (5.4)	-2.1 (-7.8 to 3.5)	.54
Proximal DVT	2 (1.6)	7 (5.4)	—	—
PE	2 (1.6)	0 (0.0)	—	—
Major bleeding or nonmajor clinically relevant bleeding	5 (4.1)	0 (0.0)	4.1 (0.4 to 9.2)	.03
Major bleeding	1 (0.8)	0 (0.0)	—	—
Nonmajor clinically relevant bleeding	4 (3.3)	0 (0.0)	—	—

fear of calf DVT should not alter full confidence in a normal D-dimer test result to identify patients who will have favorable outcomes without anticoagulant treatment.

### Recent trials and recommendations for the therapeutic management of distal DVT

**Randomized trials assessing the need for anticoagulant treatment.** To date and to our knowledge, only 5 randomized trials have assessed the need for anticoagulant treatment in patients with calf DVT.<sup>14,15,46-49</sup> The results of the fifth study,<sup>14,15</sup> the only double-blind, randomized, placebo-controlled study in this field, are presented and discussed in detail in “Is it safe not to treat distal DVT in low-risk patients?”

The first study was published >30 years ago by Lagerstedt et al.<sup>47</sup> Although the landmark study in the field, it was a small, open-label study with many methodological limitations. After a 10-day course of therapeutic heparin, 51 patients were randomized to receive either therapeutic warfarin (target international normalized ratio, 2-3) or no warfarin. During the 3-month follow-up, no patient in the warfarin arm had a recurrent VTE, whereas 19 of 28 who did not receive warfarin had recurrent VTE. However, recurrent VTE were assessed by physical examination and serial isotopic tests, which were later abandoned because of their limited sensitivity. Therefore, reliance on this single study to recommend systematic anticoagulation for all distal DVTs is difficult. Nevertheless, on the basis of this single trial and the absence of other randomized data, the 2008 American College of Chest Physicians (ACCP) consensus recommended to treat all calf DVTs with a 3-month course of anticoagulant treatment (grade 2C).<sup>50</sup>

In the second study, an open-label, randomized trial, Pinede et al.<sup>48</sup> compared a 6- vs 12-week course of oral anticoagulant treatment in patients with symptomatic DVT. Among the group of patients with distal DVT (n = 197), those who received 6 weeks of treatment had both fewer recurrent VTE (2.0% vs 3.4%; relative risk, 0.58; 95% CI, 0.1-3.36) and fewer major bleedings (1.0% vs 3.4%; relative risk, 0.29; 95% CI, 0.03-2.72) than those who received 12 weeks of treatment. Despite an open-label design, the study suggested that 6 weeks of treatment are probably enough for distal DVT.

The third randomized study focused on patients with calf muscle vein thrombosis only (ie, soleus or gastrocnemius vein thrombosis).<sup>49</sup> This study, which was not placebo controlled, randomly assigned patients to receive 10 days of subcutaneous injections of a therapeutic dose of the low-molecular-weight heparin (LMWH) nadroparin with elastic compression or to receive elastic compression alone. The study did not show significant differences in the rate of extension to proximal veins between the two groups.

The fourth randomized, open-label, feasibility study compared therapeutic anticoagulation with the LMWH dalteparin followed by warfarin with a conservative treatment (nonsteroidal anti-inflammatory drugs and/or paracetamol) in patients with calf DVT.<sup>46</sup> Seventy patients were randomized. The VTE rate was 0% (0 of 35) in the anticoagulation arm and 11.4% (4 of 35) in the conservative treatment arm. However, the small sample size and open-label design limit the robustness of conclusions that could be drawn from this study. Altogether, the analysis of these available randomized data shows a high disparity among reported results and does not allow firm conclusions to be drawn.

**Evolving international recommendations for the treatment of distal DVT.** Nevertheless, some reassuring data published in these randomized trials and in nonrandomized trials have probably had some impact on the recommendations included in international expert consensus guidelines, such as those established by the ACCP. For example, a cohort study published in 2010 in 431 outpatients in 2 Italian centers showed a low rate of proximal extension or VTE in patients left untreated for a distal DVT.<sup>51</sup> In a more recent study, 171 patients with distal DVT were treated with therapeutic LMWH for 1 week followed by half-dose LMWH for another 3 weeks.<sup>52</sup> During the treatment period, 5 (2.9%) patients had a proximal extension. Further recurrences during the rest of the 3-month observation period occurred in only 4 patients, 3 of whom had an index unprovoked event, suggesting that prolonged full-dose therapeutic treatment might not be necessary for all patients with a calf DVT.

All these data likely had an impact on the last ACCP recommendations,<sup>4,53</sup> which contrary to the recommendations of 2008, now suggest that serial imaging of the deep veins for 2 weeks could be proposed over initial anticoagulation in patients without severe symptoms or risk factors for extension. According to these recommendations, the presence of the following risk factors should warrant therapeutic anticoagulation: positive D-dimer results, extensive thrombosis or close to the proximal veins, no reversible provoking factor for DVT, active cancer, history of VTE, and inpatient status.

**Is it safe not to treat distal DVT in low-risk patients?** The next step to improve the management of distal DVT is to assess the safety of not giving anticoagulant treatment to selected patients with distal DVT at low risk for proximal extension and VTE. This was the basis to draft the Compression Alone Versus Anticoagulation for Symptomatic Calf Vein Thrombosis Diagnosed by Ultrasonography (CACTUS) trial, which is the only randomized, placebo-controlled study in the field of distal DVT.<sup>14,15</sup> In the CACTUS trial, 259 outpatients without active cancer or previous VTE were assigned to receive once daily subcutaneous injections of either the LMWH nadroparin at the therapeutic dose of 171 IU/kg or placebo for 6 weeks. The primary efficacy outcome measure was the composite

of extension of calf DVT to proximal veins, contralateral proximal DVT, or PE at 6 weeks. The primary safety outcome measure was major or clinically relevant nonmajor bleeding at 6 weeks. All patients also were prescribed elastic compression stockings for 6 weeks and followed for 90 days.

The primary efficacy outcome occurred in 4 of 122 patients (3.3%) in the nadroparin arm and 7 of 130 patients (5.4%) in the placebo arm ( $P = .54$ ; risk difference,  $-2.1\%$ ; 95% CI,  $-7.8\%$  to  $3.5\%$ ). Major or clinically relevant nonmajor bleeding occurred in 5 of 122 patients (4.1%) in the nadroparin arm and in 0 of 130 patients (0.0%) in the placebo arm ( $P = .03$ ; risk difference,  $4.1\%$ ; 95% CI,  $0.4\%$ - $9.2\%$ ) (Table 3). In the nadroparin arm, 1 patient died of metastatic cancer and 1 patient was diagnosed with type II heparin-induced thrombocytopenia. The main conclusions of the study were that the use of therapeutic doses of nadroparin for 6 weeks in low-risk outpatients with symptomatic calf DVT was not superior to placebo in reducing the risk of proximal extension or VTE but was associated with a significantly higher risk of bleeding. The main limitation of the study is that the target sample size was not reached, resulting in limited statistical power. Altogether, these studies question the necessity to treat all calf DVT with therapeutic anticoagulation.

In conclusion, whether calf DVT requires anticoagulant therapy is currently one of the most debated issues in the field of VTE. Although calf DVT is a common medical condition, only few randomized controlled trials have addressed its treatment to date. Moreover, results of these trials are discordant, with half of them suggesting that therapeutic anticoagulation should be prescribed, whereas others do not report a clear benefit. Three of these trials were open label and had many methodological limitations, whereas the only placebo-controlled trial was hampered by a limited statistical power.

Nevertheless, evidence suggests that not all calf DVTs deserve therapeutic anticoagulation. As shown in the randomized placebo-controlled trial,<sup>14,15</sup> the benefit-risk ratio of anticoagulation is highly debatable in low-risk patients. Low-risk patients (eg, those without active cancer, outpatients, and those without previous VTE) may be better served without therapeutic anticoagulation and should undergo ultrasound surveillance. This latter point supports the current ACCP guidelines, which suggest that low-risk patients with symptomatic calf DVT, such as those without a previous DVT or active malignancy, could safely be managed with serial ultrasound testing and no anticoagulant therapy.<sup>4,53</sup> Moreover, not treating all calf DVTs with anticoagulants could be an important cost-saving strategy because calf DVTs represent half of diagnosed DVTs.<sup>9</sup>

Some physicians have the empirical impression that treatment with LMWH is effective to relieve distal thrombosis-related pain. However, unpublished data of the CACTUS trial do not show a significant reduction of pain with LMWH compared with placebo.

Low-risk patients with symptomatic distal DVT may benefit more from elastic compression stockings and ultrasound monitoring than from therapeutic anticoagulant treatment. At the moment and despite the lack of clear data, continuing to give therapeutic anticoagulation to patients with active cancer, with previous VTE, and with unprovoked distal DVT seems wise.

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