Controversial Issues in the Diagnosis of Venous Thromboembolism

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Key words

Venous thrombosis · Venous thromboembolism ·
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tomography

Abstract

Although considerable progress has been made in the diagnosis of venous thromboembolism, several issues remain that are awaiting a proper solution. Among them are: the respective role of compression ultrasound of the proximal veins and ultrasonography of the entire leg vein system in the diagnostic approach of patients with the clinical suspicion of the first episode of deep venous thrombosis (DVT) of the lower extremities; the safety of managing subgroups of patients with suspected DVT without objective tests, i.e., with the use of pre-test probability scores and D-dimer assays; the role of ultrasonography in the diagnostic approach of patients with suspected ipsilateral recurrent thrombosis; and the role of spiral CT in the diagnostic approach of patients with clinically symptomatic pulmonary embolism.

Although considerable progress has been made in the diagnosis of venous thromboembolism (VTE), several issues remain that are awaiting a proper solution. I will address four of them.

Diagnosis of the First Episode of Symptomatic Deep Venous Thrombosis (DVT) of the Lower Extremities: Compression Ultrasound of the Proximal Veins vs Ultrasonography (Alone or Associated with Color-Doppler) of the Entire Leg Vein System

In this context, ascending phlebography has long represented the standard of DVT diagnosis. Because of its invasiveness, however, this test has then virtually been replaced by ultrasound imaging.

While the accuracy of compression ultrasound for detection of proximal-vein thrombosis has been convincingly demonstrated, further strategies have been validated and implemented to safely manage patients with suspected DVT irrespective of its location. Based on current information, we can say that it is safe to label symptomatic patients as not having a DVT in case of serially normal compression ultrasonography of the proximal-veins [1,2], as well as in case of a single negative test provided patients have either a low pre-test clinical probability (PTP) [3] or a negative D-dimer [4,5].

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Nevertheless, several enquiries have shown that ultrasonography of the entire leg vein system (alone or associated with color-Doppler) is the most widely employed diagnostic approach to symptomatic patients, as it has the potential to provide the imaging of (both distal and muscular) calf-veins. However, imaging of calf veins is time-consuming and technically demanding. Furthermore, although the negative predictive value of this strategy has recently been shown to be high in two small studies [6,7], the specificity of ultrasound diagnosis of calf DVT has not received proper evaluation. Finally, the clinical implications of calf DVT are unclear, and even more so are those of thrombosis of the muscular veins.

An Italian multicentre randomized study (the Erasmus study), addressing the respective role of compression ultrasound of the proximal vein system and echo-color-Doppler of the entire leg vein system in a wide series of consecutive patients referred with the clinical suspicion of the first episode of DVT is currently ongoing.

How Safe is Managing Patients with Suspected DVT without Objective Tests?

This approach is appealing, especially if we consider that objective tests are not readily available everywhere in the world. Furthermore, it has the potential to prevent an unnecessary treatment in the many patients who are candidate to ultrasound test but have to wait a few days before the objective test is performed. Finally, it is definitely cost-effective.

The safety of managing patients with suspected DVT without ultrasound tests has been convincingly demonstrated by five recent studies, all of them addressing the long-term follow-up of wide series of patients labelled as not having a venous thrombosis based on variable combinations of D-dimer and pre-test clinical probability: a low PTP and a negative SimpliRed [8], a non-high PTP and a negative D-dimer using a quantitative latex D-Dimer assay [9], a negative D-dimer alone using an ELISA [10], an ELISA D-dimer and a non-high PTP [11], and, based on the results of a recent prospective randomized study, an unlikely PTP and a negative D-dimer using either the SimpliRed or a quantitative latex D-Dimer assay [12].

Notwithstanding the safety of managing patients with suspected DVT without ultrasonography or other objective tests, these approaches are rarely adopted outside few academic hospitals. I think that lot of work still remains to be done before these strategies are more widely implemented in routine clinical practice.

Diagnosis of Ipsilateral Recurrent DVT

Long-term follow-up studies have now recognized that recurrent venous thromboembolic complications occur more frequently than previously thought. Thus, after a mean follow-up of approximately eight years in patients with a first episode of deep-vein thrombosis (DVT), one-third had developed a new confirmed venous thrombotic complication [13].

While detection of thrombosis in the previously unaffected contralateral leg does not raise diagnostic problems, diagnosis is difficult if patients present with clinical manifestations suggestive of recurrent ipsilateral DVT. Clinical diagnosis is indeed highly non-specific, and all available diagnostic strategies have serious limitations in this context. As far as the role of ultrasonography is concerned, it has been investigated in two consecutive studies performed at our Institution [14,15]. We developed a simple ultrasound method that requires repeated measurements of the diameters of the common femoral and popliteal vein in the transverse section during compression with the transducer following the first episode of DVT. On the occasion of a suspected recurrent ipsilateral DVT, the vein diameter is measured and compared with earlier ultrasound results. According to the results of our studies, in case of a stable or improved diameter, the diagnosis can be excluded provided that the test is repeated twice in a week. In case of increased vein diameter of at least 4 mm, the diagnosis of a recurrent event can be convincingly done. Finally, in case of an increased vein diameter between 2 and 4 mm, a phlebographic confirmation should be obtained. It is quite evident that a phlebographic confirmation should be obtained in all patients with positive ultrasound findings if earlier tests are not available.

The Role of Spiral CT in the Diagnostic Approach of Patients with the Clinical Suspicion of Pulmonary Embolism (PE)

Conventionally, patients with clinically suspected PE are managed with the V/Q scan. Patients with indeterminate results, who represent approximately 50% of all those who undergo this procedure, receive the ultrasound imaging of the leg vein system. In all patients with normal test, who represent more than 80%, pulmonary angiography remains the only test that can confirm or rule out diagnosis.

Of course this algorithm needs to be simplified. Spiral CT has the potential to simplify this algorithm by obviating the need for pulmonary angiography in patients with inde-

terminate V/Q scanning and negative leg veins ultrasonography, and even by obviating the need for the same lung scanning, which is so often inconclusive.

Its specificity is very high. The problem is how to interpret a negative test result, as in spite of its technological evolution spiral CT cannot accurately visualize small thrombi confined to subsegmentary arteries. Recent studies have shown that PE can be reasonably excluded in patients with

negative CT provided they have a negative CUS and low PTP [16,17], or a negative serial CUS of the legs [18].

Although a few small studies suggest that anticoagulation can be safely withheld in patients with negative result [19,20], I think that there is not yet conclusive evidence supporting the use of this test alone to confirm or ruled out PE.

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