The Role of Venous Ultrasonography in the Diagnosis of Suspected Deep Venous Thrombosis and Pulmonary Embolism

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This paper describes the role of venous ultrasonography in the diagnosis of suspected deep venous thrombosis and pulmonary embolism. Inability to compress the common femoral or popliteal vein is usually diagnostic of a first episode of deep venous thrombosis in symptomatic patients (positive predictive value of about 97%). Full compressibility of both of these sites excludes proximal deep venous thrombosis in symptomatic patients (negative predictive value of about 98%). In patients with suspected deep venous thrombosis or in those who present with suspected pulmonary embolism but have a nondiagnostic lung scan, the subsequent risk for symptomatic venous thromboembolism is very low (<2% during 6 months of follow-up) provided that ultrasonography of the proximal veins remains normal in the course of 1 week (suspected deep venous thrombosis) or 2 weeks (suspected pulmonary embolism). Anticoagulation and further diagnostic testing can usually be safely withheld in these situations. Venous ultrasonography is much less reliable for the diagnosis of asymptomatic, isolated distal, and recurrent deep venous thrombosis than for the diagnosis of a first episode of proximal deep venous thrombosis in symptomatic patients. Clinical evaluation of the probability of deep venous thrombosis or pulmonary embolism, preferably by using a validated clinical model, complements venous ultrasonographic findings and helps to identify patients who would benefit from additional (often invasive) diagnostic testing. Thus, venous ultrasonography is thought to be a very valuable test for the diagnosis and management of patients with suspected deep venous thrombosis or pulmonary embolism.

Testing for deep venous thrombosis is usually undertaken in five distinct clinical settings: 1) symptomatic patients with a suspected first episode of deep venous thrombosis, 2) symptomatic patients with a suspected recurrent episode of deep venous thrombosis, 3) patients without leg symptoms who have a high risk for deep venous thrombosis because of recent surgery (such as joint replacement), 4) patients with chronic leg symptoms or an uncertain history of deep venous thrombosis, and 5) patients without leg symptoms who have clinical features suggestive of pulmonary embolism. Venous ultrasonography is the most accurate noninvasive test for the diagnosis of deep venous thrombosis (1). However, because the size, location (proximal compared with distal veins), and prevalence of thrombi differ with the various presentations of venous thromboembolism, the accuracy and usefulness of venous ultrasonography vary according to the clinical situation (1).

In this review, we consider the strengths and weaknesses of venous ultrasonography for the diagnosis of deep venous thrombosis in patients with the five clinical presentations of suspected venous thromboembolism described above. Data were obtained from a systematic literature review of studies that evaluated venous ultrasonography for the diagnosis of deep venous thrombosis (1). Additional data were gathered through a search of the authors' personal files (with bibliographic cross-checking) to identify additional studies that evaluated the use of venous ultrasonography in patients with suspected or definite pulmonary embolism. To reduce the potential for bias, only data from prospective studies of consecutive patient series with independent (blinded) assessment of diagnostic accuracy or clinical outcomes were included (1).

We first briefly describe important technical aspects of venous ultrasonography. Differences in the reflective properties of static or moving tissues enable internal structures to be visualized and blood flow to be quantified by ultrasonography (high-frequency sound waves) (2, 3). Brightness modulation (B-mode) ultrasonography produces a real-time,

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Table 1. Positive and Negative Predictive Values of Venous Ultrasonography for Venous Thromboembolism in Different Clinical Settings*

Clinical Setting and Venous Ultrasonography Finding	Positive Predictive Value	Negative Predictive Value	Reference
	%		
Symptoms consistent with a first episode of DVT			
Abnormal proximal veins†	97	–	1
Normal proximal veins‡	–	98 (proximal DVT)	
	–	90 (all DVT)	1
Abnormal proximal veins and low clinical suspicion of DVT†	57	–	14
Normal proximal veins and high clinical suspicion of DVT‡	–	76 (proximal DVT)	14
Normal proximal veins and low clinical suspicion of DVT‡	–	99 (proximal DVT)	14
	–	98 (all DVT)	14
Abnormality of ≥2 of the common femoral, popliteal, or calf trifurcation venous sites†	100	–	20
Abnormality of 1 of the common femoral, popliteal, or calf trifurcation venous sites†	68	–	20
High risk for an asymptomatic episode of DVT (certain postoperative patients)			
Abnormal proximal veins†	74		1
Normal proximal veins‡	–	95 (proximal DVT)	1
	–	82 (all DVT)	1
Symptoms compatible with pulmonary embolism (without symptoms of DVT)			
Abnormal proximal veins and nondiagnostic lung scan†	~75	–	21

* DVT = deep venous thrombosis.
† "Abnormal" or "abnormality" refers to incomplete compressibility of the vein with the application of ultrasonographic probe pressure.
‡ "Normal" refers to complete compressibility of the vein with the application of ultrasonographic probe pressure.

two-dimensional image. Doppler techniques allow measurement of the direction and speed of blood flow. The combination of B-mode imaging and Doppler flow assessment is known as *duplex ultrasonography*. Display of the Doppler signal as a color image superimposed on the B-mode image is called *color Doppler ultrasonography*. We use the term *venous ultrasonography* to refer to any of the above techniques that include B-mode imaging of the deep veins of the leg.

The extent to which the deep venous system is examined and the criteria used to diagnose thrombosis often vary among examiners. At the least, the ability to fully compress the lumen of the common femoral and popliteal veins with the application of gentle pressure from the ultrasound probe is assessed. Full compressibility of a venous segment excludes thrombosis, whereas lack of full compressibility confirms its presence (4–8). Although they are widely used, Doppler assessment of blood flow (4, 7–9) and other B-mode criteria, such as the presence of intraluminal echoes (4–7), have not been shown to improve the diagnostic accuracy of venous ultrasonography.

First Symptomatic Episode of Deep Venous Thrombosis

Most symptomatic venous thrombi probably develop as an extension of small asymptomatic thrombi that originate in the deep veins of the calf (10–13). By the time that patients present with symptoms of deep venous thrombosis, about 85% of thrombi involve the popliteal or more proximal veins (proximal deep venous thrombosis) (4, 13–18). Venous ultrasonography is diagnostic in almost all patients who have symptomatic proximal deep venous thrombosis (sensitivity of about 95%) and is normal in almost all patients with leg symptoms who do not have thrombosis (specificity of about 96%) (1, 4, 5, 14, 19). With a prevalence of thrombosis of about 25% in symptomatic patients, approximately 97% of those who have an abnormal proximal venous ultrasonogram truly have deep venous thrombosis (positive predictive value) and therefore can be treated on the basis of this finding (1, 4, 5, 14, 19). About 98% of symptomatic patients who have a normal result on proximal venous ultrasonography truly do not have proximal thrombosis (negative predictive value); therefore, anticoagulation can be withheld, at least in the short term (1) (**Table 1**). Of symptomatic patients with a normal initial ultrasonogram of the proximal veins, about 2% of patients will have undetected proximal thrombi (generally small), and an additional 5% are expected to have isolated distal (calf) thrombi (1, 4, 5, 14, 19).

The true accuracy of venous ultrasonography for the diagnosis of isolated distal deep venous thrombosis is uncertain but seems to be considerably lower than its accuracy for proximal thrombi (sensitivity of about 73% [1]) (1, 9, 19, 22–26). Isolated distal deep venous thrombosis, in addition to being relatively uncommon (about 15% of symptomatic thrombi [1, 4, 14–18]), is rarely associated with pulmonary embolism (12, 27). Without treatment, about one quarter of isolated distal thrombi are

expected to subsequently extend into the proximal veins (12, 28, 29). Consequently, a single normal venous ultrasonogram that examines the proximal veins only does not exclude future episodes of clinically important deep venous thrombosis. However, because most symptomatic distal deep venous thrombi that subsequently extend do so within a week of presentation, a safe management approach is to withhold anticoagulation in patients with a normal initial ultrasonogram of the proximal veins and repeat the examination after 1 week (1, 26, 30). Approximately 2% of these patients will have an abnormal proximal venous ultrasonogram at the second examination; at that time, venous thrombosis can be diagnosed (1, 26, 30–32). This serial testing approach avoids time-consuming and not very accurate ultrasonography for calf vein thrombi, most of which are benign and do not need to be treated. Among patients in whom anticoagulant therapy is withheld on the basis of a normal serial venous ultrasonogram, subsequent symptomatic episodes of venous thromboembolism occur in less than 2% during 6 months of follow-up (1, 26, 30–32), a rate similar to that observed after normal contrast venography (33).

Clinical assessment in which patients are categorized as having a low, moderate, or high pretest probability of deep venous thrombosis, preferably with the use of a validated clinical model (14, 34, 35), complements the findings of venous ultrasonography (14, 34). Ultrasonography is usually accurate provided that its results and clinical assessment are concordant. However, its accuracy decreases markedly if the results of these two assessments do not agree (14) (**Table 1**). Consequently, venography should be considered if the clinical suspicion for deep venous thrombosis is low and the ultrasonogram is abnormal or if the clinical suspicion is high and the ultrasonogram is normal. In about one quarter of such cases, the results of venography differ from those of ultrasonography (14, 34). Because the prevalence of deep venous thrombosis (usually isolated distally) is only about 2% in patients in whom the clinical suspicion of this condition is low and the initial proximal venous ultrasonogram is normal, a follow-up test is not necessary (14, 34).

Almost all deep venous thrombi start in the calf and extend proximally (10–13) or, less frequently, start high in the proximal veins (such as the iliac or common femoral veins) and extend distally (13). Consequently, isolated short segments of proximal venous thrombosis are uncommon, particularly with involvement of the superficial femoral vein alone (that is, the part of the deep veins that lies between the common femoral and the popliteal veins) (13). Consistent with these observations, if venous ultrasonography is abnormal at two or more of the common femoral, popliteal, and calf trifurcation venous sites, the prevalence of deep venous thrombosis has been found to be 100%, whereas if ultrasonography is abnormal at only one of these sites, the prevalence is 68% (20) (**Table 1**). Because ultrasonographic abnormalities confined to short segments of the deep veins are often not due to acute thrombosis (that is, they have a lower positive predictive value), venography should be considered with such findings (1).

Recurrent Deep Venous Thrombosis

Diagnosis of recurrent deep venous thrombosis is made difficult by the fact that persistent abnormalities of the deep veins are common after a first episode of thrombosis. For example, venous ultrasonography of the proximal veins is still abnormal in about 50% of patients 1 year after a first episode of proximal deep venous thrombosis (36, 37). Consequently, the presence of a noncompressible venous segment on venous ultrasonography does not reliably diagnose recurrent thrombosis; evidence of new thrombus formation is necessary. Convincing venous ultrasonographic evidence of recurrent thrombosis requires documentation of a new noncompressible common femoral or popliteal venous segment or a marked increase in venous diameter during compression ($\geq$4 mm) at either of these sites compared with a previous ultrasonogram (1, 37). If the common femoral and popliteal veins are fully compressible or if the diameter of one or both veins has increased 1 mm or less compared with a previous ultrasonogram, recurrent proximal deep venous thrombosis can be excluded (1, 37). With both of these findings, two follow-up ultrasonographic examinations should be performed over 7 to 10 days to detect extending thrombosis. If an abnormal initial venous ultrasonogram shows a change in diameter of the common femoral or popliteal veins of more than 1 mm but less than 4 mm compared with a previous test or if a previous ultrasonogram is not available for comparison, the result is nondiagnostic and additional testing (such as impedance plethysmography or venography) should be considered (1).

First Asymptomatic Episode of Deep Venous Thrombosis

Venous ultrasonography can be used to detect asymptomatic deep venous thrombosis in high-risk patients after surgery but before hospital discharge. The goal is to prevent symptomatic venous thromboembolism by initiating treatment if the test result is positive. However, the accuracy of venous ultrasonography is much lower in asymptomatic patients than in symptomatic patients for several reasons

(**Table 1**) (1, 38). First, the distribution of deep venous thrombosis differs for symptomatic and asymptomatic patients: Two thirds of deep venous thrombi are confined to the calf veins in asymptomatic patients (18, 39–42), whereas this is the case in only about 15% of symptomatic patients with thrombosis (4, 13–18). Second, when proximal deep venous thrombosis is present, it is often less extensive in asymptomatic than in symptomatic patients (18). Third, asymptomatic and symptomatic thrombi may differ qualitatively; the former are likely to be of more recent onset and, therefore, may have undergone less organization, making them harder to detect (that is, less likely to show noncompressibility). Finally, venous ultrasonography may be technically more difficult to perform and interpret after the patient has undergone surgery. This is especially true after orthopedic surgery because of reduced patient mobility and surgery-related leg swelling. Consequently, venous ultrasonography fails to detect about one third of proximal deep venous thrombi seen on venography in asymptomatic postoperative patients (sensitivity of about 62%), and only about three quarters of such patients with an abnormal ultrasonogram truly have proximal deep venous thrombosis (1).

Consistent with the low accuracy of ultrasonography in this setting, convincing evidence now shows that use of venous ultrasonography to detect asymptomatic deep venous thrombosis in high-risk patients before discharge is not worthwhile if patients have received appropriate prophylaxis against venous thromboembolism (43). In a recent study of more than 1000 patients who underwent hip or knee arthroplasty and received warfarin after surgery, asymptomatic deep venous thrombi were detected and treated in 2.5% of those who were randomly assigned to undergo predischarge venous ultrasonography in contrast with no screening (43). However, after hospital discharge, the two study groups did not differ in the frequency of symptomatic venous thromboembolism (43). If effective prophylaxis cannot be used in high-risk surgical patients (for example, if antithrombotic agents are contraindicated), venous ultrasonography may have a role in surveillance testing, although the value of such an approach is uncertain (44, 45). In addition, because ultrasonography has a lower specificity in this setting, confirmatory venography should be considered in patients with an abnormal test result unless the ultrasonographic findings are unequivocal.

Chronic Leg Symptoms or an Uncertain History of Deep Venous Thrombosis

In some patients, the venous ultrasonogram remains abnormal, displaying thickening of the venous wall or incomplete compressibility, for months to years after an initial episode of deep venous thrombosis (36, 37). These persistent abnormalities may suggest that a past episode of venous thrombosis occurred in patients with chronic symptoms of leg pain and swelling or in those with a history of thrombosis diagnosed by clinical assessment alone. However, because a single ultrasonogram cannot distinguish between recent or remote thrombosis, venography is usually required to exclude the possibility of acute disease in patients with an abnormal ultrasonogram. Because the ultrasonogram is often normal in patients with a history of deep venous thrombosis, a normal test result does not exclude the possibility that current symptoms are due to previous thrombosis.

Pulmonary Embolism

Pulmonary embolism rarely occurs in the absence of preceding proximal deep venous thrombosis of the legs (which is usually asymptomatic) (46, 47). This observation has been used in an attempt to simplify the diagnostic process in patients with suspected pulmonary embolism. For example, if a ventilation–perfusion scan is abnormal but not diagnostic of pulmonary embolism, venous ultrasonography can be used to detect asymptomatic proximal deep venous thrombosis. The finding of proximal deep venous thrombosis provides indirect evidence that the patient has pulmonary embolism and requires anticoagulant therapy. A positive venous ultrasonogram is found in 5% to 10% of patients with nondiagnostic lung scans (21, 48, 49). If deep venous thrombosis is not found, it is less likely that the patient has had pulmonary embolism, but the possibility is not excluded (21, 48). In the absence of detectable proximal deep venous thrombosis, however, the risk for recurrent pulmonary embolism is low and anticoagulant therapy can be withheld in these patients, at least in the short term, while they undergo further investigation (50, 51).

About 80% of patients with suspected pulmonary embolism, a nondiagnostic lung scan, and a normal proximal venous ultrasonogram do not have pulmonary embolism (21, 48). The remaining 20% of patients with suspected pulmonary embolism who have a nondiagnostic lung scan and a normal proximal venous ultrasonogram have had pulmonary embolism and have either small residual thrombi (usually confined to the calf) or no residual thrombus. These patients are at risk for recurrent pulmonary embolism if the small residual thrombi extend or if a new thrombus forms; the period of highest risk is within 2 weeks of presentation (52–54). However, before these patients have a recurrent episode of pulmo-

Table 2. Factors That Reduce the Positive Predictive Value of Venous Ultrasonography for Acute Thromboembolism

Factor	Reference
Major	
Asymptomatic for deep venous thrombosis	1
Low clinical suspicion of deep venous thrombosis	14
Abnormality confined to a short segment of the proximal veins	20
Abnormality confined to the calf veins	1
History of previous venous thromboembolism	1
Negative result on another test that is sensitive for deep venous thrombosis (such as D-dimer)	48
Minor	
Low prevalence of deep venous thrombosis in the referral population	14

With one or more of the above major factors, additional diagnostic testing (such as venography) should be considered to exclude the possibility of a false-positive result.

nary embolism, they must first redevelop proximal deep venous thrombosis. Performance of serial venous ultrasonography over 2 weeks enables patients who are progressing toward recurrent pulmonary embolism to be identified and treated before recurrent embolism (50, 51). To identify patients who are progressing toward recurrent pulmonary embolism, it is necessary to perform serial ultrasonography in all patients with suspected pulmonary embolism, a nondiagnostic lung scan, and a normal initial proximal venous ultrasonogram if pulmonary angiography is not performed. With this management approach, about 2% of patients have an abnormal proximal venous ultrasonogram during serial testing (49, 51). Patients with nondiagnostic lung scans who do not have an abnormal ultrasonogram during serial testing are expected to have a low subsequent risk for symptomatic deep venous thrombosis or pulmonary embolism (<2% during 6 months of follow-up) (49, 51).

Use of serial venous ultrasonography to manage patients who have suspected pulmonary embolism and a nondiagnostic lung scan has some limitations. The accuracy of ultrasonography for the diagnosis of thrombosis in patients with suspected pulmonary embolism but no symptoms of deep venous thrombosis seems to be similar to the accuracy for the diagnosis of asymptomatic deep venous thrombosis in postoperative patients (positive predictive value of about 75%) (1, 21) (**Table 1**). Consequently, treatment of all such patients with an abnormal venous ultrasonogram will result in inappropriate anticoagulation in about 2% of patients with nondiagnostic lung scans (21). This risk can be minimized by performing venography or pulmonary angiography in patients with less convincing ultrasonographic evidence of thrombosis (**Table 2**). In addition, the use of serial noninvasive testing for deep venous thrombosis in patients with suspected pulmonary embolism has been inadequately evaluated in two patient groups: those with poor cardiopulmonary reserve (51) and those with a high clinical suspicion of pulmonary embolism (49) (70% prevalence of disease [55, 56]). Therefore, it may not be safe to use the serial testing approach in these patient groups.

Conclusion

Venous ultrasonography is a valuable test for the diagnosis and management of patients with suspected deep venous thrombosis and pulmonary embolism. However, to use venous ultrasonography optimally, the natural history of venous thromboembolism and the limitations of the technique need to be fully understood and appreciated, and the results of ultrasonography must be integrated with other pertinent clinical and laboratory information.

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