

Editorial Focus

Safety of venous ultrasound in suspected DVT – still a matter of concern?

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Although venous ultrasound has been introduced into clinical practice more than 20 years ago there is ongoing debate about accuracy, reproducibility and the best scanning protocol to rule out deep venous thrombosis (DVT).

In 1989 Lensing et al. (1) published a comparison between ultrasound and venography of 220 consecutive patients with clinically suspected DVT. They defined compression ultrasound as an examination technique, where application of a compression manoeuvre with the ultrasound transducer to patent veins leads to their collapse. A thrombus is detected, if the vein is not fully compressible. Using this technique the authors found an overall sensitivity and specificity of 91% for compression ultrasound. Sensitivity and specificity were even higher (100% and 99%, respectively) in the case of proximal DVT, as documented by venography. Furthermore, an excellent inter-observer agreement proved reproducibility of test results. Subsequently, Cogo et al. (2) compared compression ultrasound versus Doppler ultrasound in a series of 158 patients with clinically suspected DVT and used venography as the gold standard. While both ultrasound protocols were highly specific (100% vs. 98%), compression ultrasound proved to be more sensitive (100%) compared to Doppler ultrasound (76%). Further studies confirmed these findings and all together lead to the conclusion that B-mode compression ultrasound is superior to other ultrasound modalities.

However, the important question as to whether anticoagulant treatment can be safely withheld in patients based on a negative ultrasound testing alone still remained unsettled. One of the first studies to address this topic was published by Cogo et al. in 1998 (3) and included 1,702 patients with suspected DVT. The examination protocol consisted of compression manoeuvres of groin and popliteal region to detect proximal DVT. As segmental thrombi of the thigh veins or isolated calf veins would have been missed during first examination, patients with initially negative findings were re-examined after one week to detect a propagation of untreated segmental thrombi into groin or popliteal veins. This concept of repeated ultrasound testing after an initial

negative result proved to be safe with a rate of symptomatic venous thromboembolism (VTE) of 0.7% during a six-month follow-up. Practicability of this approach, however, is restricted by the high number of repeated testing: in the study by Cogo et al. (2) about 1,300 patients had initially negative ultrasound scans and had to be retested. Furthermore, some patients with normal initial examination received anticoagulant therapy despite normal ultrasound findings or underwent venography, demonstrating a lack of trust in the result of the initial examination.

Since then serial testing with a segmental ultrasound protocol has been used in several further trials and has become daily routine in many hospitals. The need of repeated testing of all initially negative patients, however, is cumbersome, cost-ineffective (4) and patients have to be kept in uncertainty about the exact diagnosis for one week.

Therefore, a single test using complete compression ultrasound (cCUS) of the whole deep venous system of the leg starting from the groin down to the ankle including calf veins and calf muscle veins was suggested as an alternative protocol. Schellong et al. published a retrospective outcome study in 2001 (5), showing a 0.9% incidence of symptomatic VTE events during follow-up after a negative cCUS test for suspected DVT in 214 patients. Shortly afterwards, two groups independently performed prospective monocentric trials using a single cCUS examination to rule out DVT. Of note, both trials were published in the same issue of *Thrombosis and Haemostasis* in 2003. Schellong et al. (6) followed 1,023 cCUS-negative patients for three months and found an incidence of symptomatic VTE of 0.3%. Using the same study protocol Elias et al. (7) found a 0.5% rate of symptomatic VTE during follow-up in 401 patients with negative cCUS during first presentation. Later on similar trials were published in 2004 by Stevens et al. (8) and 2005 by Subramaniam et al. (9), with event rates of 0.8% and 0.24%, respectively.

The concept of compression ultrasound proved to be a valuable tool to diagnose or safely rule out DVT in a number of clinically relevant situations: Le Gal et al. (10) evaluated the sensitivity and specificity of compression ultrasound in a series of 756 pa-

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tients with suspected pulmonary embolism (PE). They found a specificity of 99% for positive compression ultrasound to predict PE, whereas sensitivity was only 39%. They concluded that compression ultrasound is valuable to diagnose PE without further examinations in suspected patients. In addition, Prandoni et al. (11) evaluated the safety of withholding anticoagulant therapy in patients with suspected DVT in a previously affected leg. They compared residual vein diameters of the common femoral and popliteal vein under compression with data from earlier examinations and repeated this testing on day 2 and 7. Therapy was withheld in 150 patients with stable or improved findings, and VTE complications occurred in 1.5% of these patients during six months of follow-up.

Based on the available data there is some consensus that compression ultrasound, using either segmental ultrasound protocols with repeated testing or a single test using the cCUS protocol by experienced examiners, is accurate to either exclude or diagnose DVT in symptomatic patients.

However, there is a serious limitation to this. The available data on the safety of withholding anticoagulant therapy in cCUS-negative patients with suspected DVT are derived from large cohorts of patients, which were examined in tertiary care centres specialised in cCUS examinations and involving only a few specially trained sonographers. Most patients with suspected DVT are seen in the ambulatory setting, for which cCUS safety data are not available.

In this issue of *Thrombosis and Haemostasis* Sevestre et al. (12) present an important study in the field of venous ultrasound, providing safety data on a sample of 1,254 patients with negative cCUS seen by 255 vascular physicians practicing in private offices throughout France. These patients were a subgroup of the OPTIMEV study investigating 3,871 patients with suspected

DVT by a standardised cCUS protocol. Of 2,848 patients with initially negative test result a random sample of 1,254 patients were further studied prospectively. In these patients anticoagulant treatment was withheld and a three-month follow-up conducted to determine the incidence of symptomatic VTE. Among the 1,243 patients available for statistical analysis the rate of symptomatic DVT was 0.5%. This low rate of symptomatic DVT after single negative cCUS examination is in accordance with all previous large cohort studies conducted in specialised centres. Therefore, it can be concluded that the safety of cCUS to rule out DVT is not limited to the somewhat artificial world of clinical trials performed in selected, highly specialised centres, but can be reproduced in daily routine of vascular physicians working in an outpatient setting. It has to be pointed out, however, that the vascular physicians that participated in the trial were trained in performing a standardised cCUS protocol.

In conclusion, venous compression ultrasound, performed either using limited ultrasound protocols with repeated testing or a single test using the cCUS protocol, is highly accurate to exclude DVT in symptomatic patients with suspected DVT or recurrent DVT, in tertiary care centers as well as in an ambulatory setting. Anticoagulant treatment can be safely withheld in patients with negative test results, if the sonographer has been trained and is applying a standardised ultrasound protocol. Nonetheless, further studies are still needed on the topic of distal DVT, where there is ongoing debate on the clinical impact and therefore, on the need to examine calf veins. Finally, the accuracy of compression ultrasound protocols in asymptomatic patients is still a matter of concern (13, 14), since cCUS results may be less reliable in screening situations than in symptomatic patients. Improvement in ultrasound techniques and further standardisation could be necessary to overcome this limitation.

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