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Clinical aspects of recurrent venous thromboembolism

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High percentage of non-diagnostic compression ultrasonography results and the diagnosis of ipsilateral recurrent proximal deep vein thrombosis

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ABSTRACT

Establishing a diagnosis of recurrent deep vein thrombosis (RDVT) by compression ultrasonography (CUS) is often difficult because persistent abnormal findings of the deep veins are common after a first episode of DVT. This may lead to a high percentage of potential misclassified patients with ipsilateral RDVT. The objective of the study is to evaluate the diagnostic management of ipsilateral RDVT by CUS in daily practice.

This study was a retrospective cohort study of 90 consecutive patients, who had a CUS because of clinically suspected ipsilateral RDVT. The medical records and CUS reports were reviewed according to established diagnostic CUS criteria for RDVT. During the study period, in 52 of the 90 patients (58 %) the diagnosis was accurately ruled out and anticoagulant treatment was withheld. According to our predefined criteria in only 9 patients (10%) the diagnosis of ipsilateral RDVT could be definitively established. In the remaining 29 patients (32%) the criteria of RDVT were not met by documentation in reports and a definitive diagnosis could not be made. In 29 out of 90 patients (32 %) who had a CUS because of a suspected ipsilateral RDVT, the diagnosis could not be reproduced with certainty by reviewing the CUS reports according to the predefined criteria. This high percentage of non-diagnostic CUS indicates the urgent need for more accurate diagnostic methods in patients presenting with suspected ipsilateral RDVT.

INTRODUCTION

The diagnostic management of patients presenting with a clinically suspected ipsilateral recurrent deep vein thrombosis (RDVT) represents a challenge for clinicians. Objective diagnostic testing is mandatory, a clinical diagnosis being unreliable because of insensitive and nonspecific clinical signs and symptoms.¹ Up to two-third of patients presenting with new leg symptoms do not have RDVT, but other non-thrombotic disorders which do not require anticoagulant treatment, including symptoms of a post-thrombotic syndrome.² Contrast venography, the reference method for the diagnosis of acute DVT, often does not allow the visualization of a new intraluminal filling defect in vessels that have been obliterated by a previous thrombotic process. Furthermore contrast venography is now seldom used anymore. Compression ultrasonography (CUS) has a high accuracy for a first episode DVT, and test procedures are usually simple and reproducible.³ Non-compressibility of the common femoral vein, the popliteal vein or both is diagnostic for proximal DVT (sensitivity of 95%, specificity of 96%).^{1,4} Although a first episode of DVT can be reliably diagnosed, the establishment of the diagnosis of ipsilateral RDVT by CUS remains challenging. Lack of venous compressibility on CUS examination can be caused by either a RDVT, or an incomplete resolution of the initial thrombus.⁵ Differentiation between these two entities is clinically important because only an acute RDVT requires anticoagulant treatment. For the diagnosis of a RDVT different CUS criteria are established.⁴⁻⁶ Recurrent DVT is defined as a new non-compressible venous segment on CUS, a non-compressible normalized venous segment or an increase of more than 4 mm of thrombus mass in a previously involved venous segment.⁴⁻⁶ Previous studies have validated these criteria for the diagnosis of RDVT by CUS, but there is a lack of data in the literature reporting the daily practice of diagnosing clinically suspected ipsilateral RDVT.⁴⁻⁶ The purpose of this study was to evaluate daily practice patterns in the diagnostic management of clinically suspected ipsilateral RDVT. Furthermore we evaluated the management consequences of the CUS test results. Our hypothesis is that in daily practice an over diagnosis of ipsilateral RDVT takes place and that therapeutic management decisions are often made based on non-diagnostic CUS.

PATIENTS AND METHODS

Patients

All consecutive patients who had a CUS because of a clinically suspected, ipsilateral RDVT at the Leiden University Medical Centre, Leiden, the Netherlands. Patients were included during a 2-year period from January 1st 2002 until December 31st 2003.

Compression ultrasonography report findings

Compression US report findings were classified as negative for RDVT if both the common femoral vein and the popliteal vein were fully compressible. The diagnostic criteria of RDVT were a new non-compressible segment on CUS, a previous normalized vein that had become non-compressible, or an increase of more than 4 mm in thrombus diameter of a previously involved and still non-compressible venous segment.⁴⁻⁶

Study Design

This study was a retrospective cohort study of 90 consecutive patients who had a CUS because of a clinically suspected acute ipsilateral RDVT. All CUS reports of these patients during the study period and the available CUS reports from earlier episodes of DVT were systematically and individually reviewed. Reports were evaluated according to the previously described criteria for a recurrent event. All the demographic characteristics of the included patients were collected by reviewing patients' medical records and by contacting patients' general practitioners. Finally patients' anticoagulant therapy regimes were assessed.

Data –handling and analysis

All patients' data and the CUS report reviews were coded and stored in a computerized database. Patients were categorized as treated or not treated as a RDVT and the different proportions of the study population were calculated after reviewing the CUS reports.

RESULTS

Study patients

From January 1st 2002 until December 31st 2003, 118 consecutive patients with clinically suspected RDVT had a CUS at the Leiden University Medical Center. Twenty-eight patients (24%) were not eligible for the study because they had a clinically suspected RDVT of the contralateral leg. Therefore our analysis included 90 patients. The main demographic and clinical characteristics of the study patients are shown in Table 1.

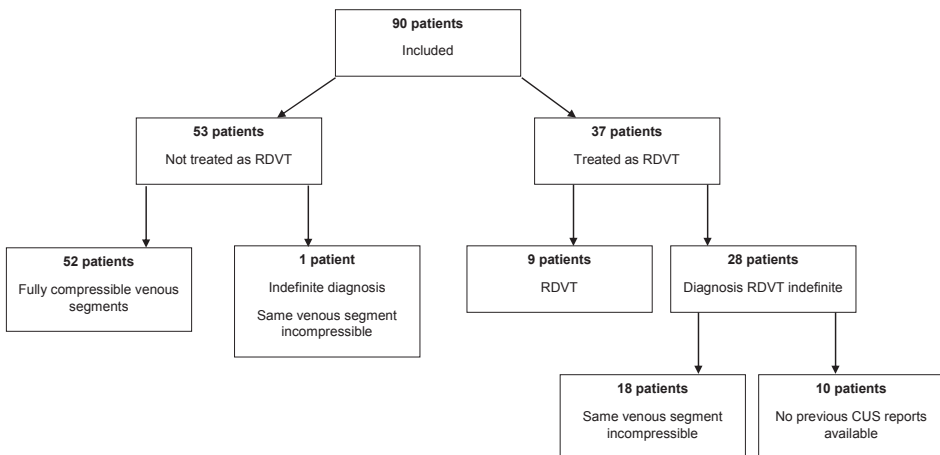
CUS reports

All CUS reports were collected in the included 90 patients. As shown in Figure 1, out of these 90 patients, in 53 patients (59%) the diagnosis RDVT was ruled out. Fifty-two patients had a fully compressible common femoral or popliteal vein segment on CUS. One patient had a non-compressible venous segment. According to the radiologist this patient had a persistent residual thrombosis from the previous episode. However no thrombus diameter during full compression had been measured and no CUS has been

Table 1. Demographic characteristics of patients.

Patients (n)	90
Age (median, range)	48 (16-88)
Sex (% males)	30%
Localization (% left leg)	63%
Interval between the last episode of DVT and suspected recurrence (n = 90)	
0 to 6 months	20 %
7 to 12 months	11 %
13 to 24 months	10 %
Longer than 24 months	59 %
Interval between the last episode of DVT and the diagnosis of ipsilateral RDVT (n=37)	
0 to 6 months	27 %
7 to 12 months	6 %
13 to 24 months	5 %
Longer than 24 months	62 %

n: number; DVT: deep vein thrombosis; RDVT: recurrent deep vein thrombosis

**Figure 1.** Overview of the results

performed between the recurrent event and previous episode. So we are not informed whether the thrombus diameter had increased or whether the CUS had been normalized after the previous episode. The remaining 37 patients (41%) were diagnosed as having ipsilateral acute recurrent DVT. In 9 of these 37 patients a diagnosis of RDVT could be established, either on the basis of a new non-compressible segment (3 patients) or because a previous normal(ized) vein had become non-compressible (6 patients). In the other 28 patients there was uncertainty in the diagnosis of acute RDVT: in 10 of these 28 patients no earlier CUS reports were available to make a proper determination between

a residual DVT and an acute RDVT. In the other 18 patients the discrimination between a residual DVT and RDVT was unreliable, because the same previously involved venous segment was still fully incompressible.

Treatment decisions

In 46 of 53 patients in whom ipsilateral DVT had been ruled out, anticoagulant treatment was withheld, while in seven patients anticoagulation therapy was continued. These seven patients had their suspected episode during the anticoagulant therapy of their previous episode. All of the 37 patients who were diagnosed as an ipsilateral RDVT were treated with anticoagulant therapy with a varying duration from 3 months to lifelong therapy.

DISCUSSION

This study shows that in 29 out of 90 patients (32%) who had a CUS because of a clinically suspected acute ipsilateral RDVT, the diagnosis could not be made with certainty by reviewing CUS reports with established criteria of ipsilateral RDVT. The diagnostic limitation is mainly present in patients presenting with a suspected ipsilateral RDVT, who have an incompressible venous segment. Diagnosing RDVT based on these criteria was only possible in 9 of the 37 patients, who were initially treated as an acute ipsilateral RDVT. Two reasons for this high percentage of non-diagnostic CUS can be given. First, in 10 patients earlier CUS information was unavailable to make a proper determination between a residual vein thrombosis and a RDVT. Radiologists need detailed information about previous episodes to make a proper discrimination between a RDVT and a residual vein thrombosis. In daily practice this is often not possible, because CUS reports are frequently not available (anymore) and patients do not return to the same hospital. Furthermore the reports are often not detailed enough to make a comparison between the examinations. Second, in 19 patients the same previously involved segment was still incompressible. This renders discrimination between a new event and a residual abnormality uncertain. In the material we have reviewed routine measurement of the thrombus diameter was not performed. Although often recommended in guidelines the validity of diagnosing RDVT using change in thrombus diameter can be debated because of high inter- and intraobserver variability.^{4,7} A possible solution to overcome the limitations of CUS is performing an additional CUS directly after discontinuation of anticoagulant therapy. With these examinations baseline images can be obtained. A recent study showed that in 8 of the 284 patients in whom recurrent venous thromboembolism (VTE) had been excluded and treatment was withheld a VTE event occurred in the 90-day follow-up (2.8%; 95% CI, 1.4-5.5%). In this study however only a

small number of patients with a clinically suspected ipsilateral RDVT (42 patients) were included, therefore it remains unclear whether anticoagulant therapy could be safely withheld in patients with an unchanged residual thrombosis. Furthermore performing an additional CUS is time consuming, associated with costs and does not overcome the observer variability of thrombus measurement in case of an incompressible venous segment. Nevertheless, the availability of a reference CUS examination has the potential to improve the diagnostic work-up for patients with suspected ipsilateral RDVT.⁸

A limitation of our study was the dependency on CUS reports rather than CUS images. Compression US is a dynamic test and has optimal diagnostic characteristics when directly interpreted by the operator. The dynamic images are stored as non-dynamic test results and have limitations when used for re-evaluation. This limitation also accentuates once more a problem radiologists face in daily practice and emphasizes the importance of accurate and detailed diagnostic reports. Recently a study using Magnetic Resonance Direct Thrombus Imaging (MRDTI) evaluated the MR signal change over 6 months.⁹ This method is based upon the paramagnetic properties of methemoglobin. The abnormal MR signal indicating an acute thrombosis had vanished after 6 months of the acute DVT event, while 31% of the patients still had an abnormal CUS examination. This study indicates that MRDTI may potentially be an accurate method to distinguish a new recurrent event from an old thrombus in patients with acute suspected RDVT. However, this has to be evaluated in prospective management studies.

In conclusion, this study showed that the use of the established diagnostic criteria of CUS is less clinical applicable in the daily diagnostic work-up of suspected ipsilateral RDVT. The associated high percentage of non-diagnostic CUS and related overdiagnosis and overtreatment indicates the urgent need for more accurate diagnostic methods and strategies in patients presenting with suspected ipsilateral RDVT.

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