Accuracy of compression ultrasound in screening for deep venous thrombosis in acutely ill medical patients

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Summary
The value of vein ultrasonography for diagnosis of symptomatic deep vein thrombosis (DVT) is widely accepted. We are unaware of published data comparing ultrasonography with the “gold standard” of venography for DVT diagnosis in asymptomatic persons in the patient group of acutely ill medical patients. It was the objective of this study to evaluate sensitivity and specificity of compression ultrasound (CUS) examinations in the diagnosis of proximal and distal DVT in acutely ill medical patients with congestive heart failure (NYHA class III and IV), exacerbations of respiratory disease, infectious disease, and inflammatory diseases considered to be at moderate risk of venous thromboembolism (VTE). CUS examination was performed prior to ascending venography on day 6–15 of the hospital stay. Both investigations were done on the same day, each interpreted without knowledge of the other’s result. Proximal and calf veins were separately evaluated. Technically satisfactory venography was obtained in 160 patients. In 12 of 160 patients (7.5%, 95% CI = [4.0%-12.7%]), venography confirmed the presence of DVT, all of which was asymptomatic. Proximal DVT was detected in five patients (3.1%, 95% CI = [1.0%-7.1%]) and distal DVT in seven patients (4.4%, 95% CI = [1.8%-8.8%]). CUS of proximal veins was technically satisfactory in all 160 patients and CUS of distal veins in 150 patients. In three of five patients with venographically proven proximal DVT, the diagnosis was confirmed by CUS (sensitivity 60%, 95%CI = [23%-88%]). In one patient, the CUS was false positive (specificity 99.4%, 95%CI = [96%-99%]). Positive and negative predictive values (PPV and NPV) of CUS in the diagnosis of proximal DVT were 75% (95%CI = [30%-95%]) and 98% (95% CI = [95%-99%]), respectively. In two of seven patients with veinographically proven calf DVT, the diagnosis was confirmed by CUS (sensitivity 28.6%, 95%CI = [8%-64%]) and in two patients, CUS was false positive (specificity 98.6, 95%CI = [95%-99%]). PPV and NPV of CUS in diagnosis of distal DVT were 50% (95%CI = [15%-85%]) and 96% (95% CI = [92%-98%]), respectively. In conclusion, CUS underestimated the incidence of proximal and distal DVT compared to contrast venography in acutely ill medical patients without thrombosis symptoms.

Keywords
Venous thromboembolism (VTE), deep vein thrombosis (DVT), compression ultrasound (CUS), venography

Introduction
Venous thromboembolism (VTE) is an important complication among acutely ill medical patients and can be fatal due to pulmonary embolism (PE). Although the risk without prophylaxis of all VTE was 15% in one study of medical inpatients, MEDENOX, the rate of clinically symptomatic DVT was only 6% (1). The rate of all VTE in the placebo arm of a second study of medical inpatients, PREVENT, was only 5%, while the rate of clinically symptomatic VTE was only 1.4% (2). Part of the explanation for such different VTE rates in these studies is probably related to the methods used for DVT diagnosis. In 83% of patients in the MEDENOX study (1), the diagnosis of VTE was made by bilateral contrast venography (in the remainder by ultra-
sonography), but in the PREVENT study it was made solely by compression ultrasound (CUS).

Although the use of ultrasonography as a diagnostic procedure for DVT in screening asymptomatic medical patients is becoming increasingly accepted (3), we are unaware of any published data comparing venous ultrasonography with the "gold standard" of venography in the acutely ill medical patient group. In postoperative orthopedic surgery patients without thrombosis symptoms, ultrasound is far less sensitive, specific, and predictive compared to venography (4, 5).

The aim of our study was to evaluate the accuracy of CUS examinations in the diagnosis of proximal and distal DVT of the lower extremities relying on contrast venography as the comparison standard for diagnosis of DVT. We took advantage of a study population of at-risk acutely ill medical patients participating in a placebo-controlled clinical trial of VTE prophylaxis, who had consented to bilateral lower extremity venography.

**Patients and methods**

This study was performed between April 2002 and March 2003 at the National Tuberculosis and Lung Disease Research Institute in Warsaw, Poland. The local Ethical Committee reviewed and accepted the protocol of the double-blind prophylaxis study as well as our diagnostic accuracy study.

**Study population**

After providing informed consent, consecutive acutely ill medical patients entered this study. In 160 of 170 patients, ascending venography was technically satisfactory. All patients were hospitalized due to congestive heart failure (CHF) – (NYHA class III and IV) or respiratory, infectious or inflammatory diseases, or some combination of these conditions. Patients with VTE objectively documented at presentation were excluded. Half of the study patients received active pharmacological prophylaxis for VTE (fondaparinux, 2.5 mg sq once daily); the other half received identical-appearing placebo injections. All enrolled patients were considered at moderate risk of VTE.

**Compression ultrasonography (CUS)**

Bilateral CUS examination of the lower extremities (equipment: Sequoia C 256, linear probe with pulse and color Doppler) was performed, prior to venography by highly skilled physicians (who have participated in many international, clinical trials used CUS for DVT diagnosis). Examinations were recorded and reassessed by two radiologists.

Bilateral contrast venography was scheduled on day 6–15 of the hospital stay at the end of the course of the blinded prophylaxis study drug. Both investigations (CUS and venography) were performed on the same day and interpreted without knowledge of the other. The proximal and calf veins were evaluated. The primary criterion for diagnosing DVT was loss of venous compressibility. The common femoral vein and femoral vein were examined with the patient in a supine position. For better visualization, the lower extremities were rotated externally. The veins were evaluated as distally as possible in both transverse and longitudinal position. To examine the popliteal vein, the patient was in either supine or prone position with the knees slightly flexed. When in prone position, the legs were supported by the examiner’s fingers. Our study also evaluated the calf veins. Peroneal, anterior tibial, and posterior tibial veins were examined. Imaging of the calf was performed in supine position with knees flexed. External rotation was employed if necessary, especially for examination of peroneal veins. The veins were identified above the ankles and followed superiorly as far as possible. A vein was considered positive for DVT when non-compressible.

**Venography**

Bilateral ascending contrast venography was performed after the injection of non-ionic low osmolar contrast (70–100 ml) into a dorsal vein on the foot. The patient was placed on a tilt table in a semi-upright position. A loose ankle tourniquet could be used to obtain optimal filling of the deep veins. The examination was considered adequate when all required deep veins (peroneal, anterior tibial, posterior tibial [pairs of veins for each], popliteal, superficial femoral, common femoral, and iliac veins) were demonstrated. The venograms were interpreted to consensus by two independent experienced radiologists who were without knowledge of the results of compression ultrasonography. An intra-luminal filling defect visualized in at least two projections was considered as positive for detection of DVT.

**Statistical analysis**

Clots found below the distal origination of the popliteal vein were counted as distal; all other were considered proximal. Statistical analysis used conventional definitions of sensitivity and specificity, negative and positive predictive value (NPV and PPV).

<table>
<thead>
<tr>
<th>No of patients</th>
<th>Mean age (years)</th>
<th>Range (years)</th>
<th>M/F</th>
<th>BMI</th>
</tr>
</thead>
<tbody>
<tr>
<td>160</td>
<td>70.5 ± 13</td>
<td>60–89</td>
<td>70/90</td>
<td>28.5 ± 10.5</td>
</tr>
</tbody>
</table>

**Table 1: Demographic variables for study patients.**

<table>
<thead>
<tr>
<th>CHF</th>
<th>Infectious exacerbation of COPD</th>
<th>Pneumonia</th>
<th>Urinary tract infection</th>
<th>Acute bronchitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>15</td>
<td>(9.4%)</td>
<td>120 (75%)</td>
<td>21 (13.1%)</td>
<td>1 (0.63%)</td>
</tr>
</tbody>
</table>

**Table 2: Main reasons for hospitalizations.**
Results

Technically satisfactory venography was obtained in 160 of the 170 patients who consented. Demographic variables for study patients are displayed in Table 1 and the main reasons for hospitalisation are summarised in Table 2.

Overall, in 12 of 160 patients (7.5%, 95% CI = [4.0%–12.7%]), venography confirmed the presence of DVT. In all 12, the DVT was asymptomatic. Among them, proximal DVT was detected in five patients (3.1%, 95% CI = [1.0%–7.1%]), and distal DVT in seven patients (4.4%, 95% CI = [1.8%–8.8%]).

In all 160 patients, CUS of proximal veins was technically satisfactory. In three of the five patients with venography-proven proximal DVT, the diagnosis was confirmed by CUS (sensitivity 60%; 95% CI = [23%–88%]). In one additional patient, the result of CUS was false positive (specificity 99.4%, 95% CI = [96%–99%]) (Table 3). In one patient in whom venography showed bilateral proximal vein DVT (common femoral and superficial femoral), CUS detected only unilateral, proximal vein DVT (the common femoral vein clot). If veins rather than patients were the denominator, the sensitivity of CUS would decrease to 50% (3 confirmed by CUS proximal DVT of 6 proximal DVT confirmed by venography).

PPV and NPV of CUS in the diagnosis of proximal DVT were 75% (95% CI = [30%–95%]) and 98% (95% CI = [95%–99%]), respectively.

In 10 of 160 patients, calf CUS was technically insufficient. None of these 10 patients had distal DVT by venography and no VTE events were observed in their follow-up. In two of seven patients with venography-proven calf vein thrombosis, the diagnosis was confirmed by CUS (sensitivity 28.6%, 95% CI = [8%–64%]), and in two patients with normal venography, CUS was false positive (specificity 98.6%, 95% CI = [95%–99%]) (Table 4). PPV and NPV of CUS in diagnosis of distal DVT were 50% (95% CI = [15%–85%]) and 97% (95% CI = [92%–98%]), respectively.

In all true-positive cases identified by CUS, the site of DVT was the same as the site identified by venography.

Discussion

Despite a relatively modest patient number and low incidence of DVT in our study, the quantities were large enough to show the relative insensitivity of CUS compared to contrast venography for identifying proximal DVT and overall DVT in acutely ill medical patients without thrombosis symptoms. Our methodology was rigorous (blinded interpretation, consecutive patients) which suggests our results are robust and generalizable. Moreover, they appear to be quite similar to what has been reported for postoperative orthopedic surgery patients undergoing CUS, duplex ultrasound, and color Doppler ultrasound (4, 5). CUS was found to have a sensitivity of 83% for detecting asymptomatic VTE in a cohort of postoperative hip and knee replacement patients, but the predictive value of a positive test was only 71% (6). In another study in which CUS was used to determine whether warfarin should be discontinued as prophylaxis following discharge after joint replacement surgery, a normal CUS appeared promising for this purpose, but the authors cautioned that a controlled trial of this strategy should be performed before its acceptance (7).

A limitation of our study is the documented, relatively low DVT event rate and that we used venous compression as the only criterion for determining the presence of DVT.

The overall low rate of DVT in our study reflects epidemiological data regarding the rate of VTE in acutely ill medical patients (taking into account information that one half of eligible patients received antithrombotic prophylaxis) (1, 2).

It is possible that the inclusion of Doppler signals and certain maneuvers increases the accuracy of ultrasonography, particularly in an expert center when symptomatic DVT is suspected (8). However, this is a hypothesis awaiting proof in asymptomatic patients undergoing ultrasonographic screening for DVT.

Our results suggest that CUS evaluation of asymptomatic at-risk medical patients to measure the thrombosis incidence or prevalence, especially in the calf, may provide false positives and an important failure of sensitivity. These results in medical patients may be at variance with a recently published meta-analysis which found that when proximal and distal lower extremities were examined in asymptomatic postoperative orthopedic patients, ultrasound far more frequently identified patients confirmed to have DVT than those confirmed to be without it (9). Moreover, we report sensitivity rather than relative likelihood of success versus failure of diagnosis.

We conclude that CUS has inferior sensitivity and lower positive predictive value compared to contrast venography for identifying proximal DVT and overall DVT in acutely ill medical patients without thrombosis symptoms. CUS would not seem useful clinically for screening individual patients and rather should not be used to identify absolute rates of thrombosis in such patients.
References