Predictive Value of Compression Ultrasonography for Deep Vein Thrombosis in Symptomatic Outpatients

Clinical Implications of the Site of Vein Noncompressibility

Brian G. Birdwell, MD; Gary E. Raskob, PhD; Thomas L. Whitsett, MD; Sherri S. Durica, MD; Philip C. Comp, MD, PhD; James N. George, MD; Timothy L. Tytle, MD; Willis L. Owen, PhD; Patrick A. McKee, MD

Background: Compression ultrasonography has a high negative predictive value for deep vein thrombosis in symptomatic outpatients. Limited data are available on factors influencing positive predictive value. The objective of this study was to evaluate the positive predictive value of compression ultrasonography according to the anatomic site of vein noncompressibility.

Methods: We performed a prospective cohort study of 756 consecutive outpatients with suspected first-episode deep vein thrombosis. Compression ultrasonography was performed at the initial visit: results were abnormal if a noncompressible segment was identified or normal if all segments were fully compressible. Venography was performed in patients with abnormal compression ultrasonography results. Positive predictive value was determined according to the site of noncompressibility: common femoral vein only, popliteal vein only, or both sites. Venography was the reference standard for the presence of deep vein thrombosis.

Results: Positive predictive value was 16.7% (95% confidence interval, 0.4%-64.1%) for noncompressibility isolated to the common femoral vein compared with 91.3% (95% confidence interval, 72.0%-98.9%) for the popliteal vein only and 94.4% (95% confidence interval, 72.7%-99.9%) for both sites (P < .001). Of 15 patients with isolated noncompressibility of the common femoral vein, 8 (53%) had pelvic neoplasm or abscess compared with 2 (5%) of 42 with noncompressibility of the popliteal vein only and 6 (13%) of 47 with noncompressibility of both sites (P < .001).

Conclusions: The positive predictive value of noncompressibility isolated to the common femoral vein is too low to be used alone as the diagnostic end point for giving anticoagulant therapy. Noncompressibility isolated to the common femoral vein is a diagnostic marker for pelvic disease.

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Ultrasonography using vein compression is widely used in the diagnostic workup of patients with leg symptoms compatible with deep vein thrombosis.\(^1,2\) Compression ultrasonography has a high negative predictive value (99%) in symptomatic outpatients when the results are normal for a test at the initial visit and for a single repeated test 5 to 7 days later.\(^3,4\) A high positive predictive value (>90%) has been reported for abnormal results obtained from compression ultrasonography of the popliteal fossa and the common femoral vein in the groin.\(^1,2,5,6\) Heijboer et al\(^6\) reported a higher positive predictive value for compression ultrasonography (94%) than for impedance plethysmography (83%) when these tests were compared in a randomized trial of symptomatic outpatients. The causes of false-positive results of impedance plethysmography are well documented and are usually readily identified in the history and physical examination.\(^7,8\) The lack of need to examine the patient for causes of false-positive test results is considered an advantage of compression ultrasonography.\(^9\) However, limited data are available on the clinical features that may contribute to false-positive results and a decreased positive predictive value. These data are important for clinicians who wish to apply the results of compression ultrasonography in their own clinical setting.

The objectives of this article are to report new data on the positive predictive value of compression ultrasonography results according to the anatomic site of noncompressibility and to describe the clinical features of patients with false-positive results. We also provide expanded data on the safety of withholding anticoagulant treatment in patients with normal results of compression ultrasonography.
PATIENTS AND METHODS

PATIENTS AND STUDY PROTOCOL

We studied 756 consecutive outpatients with suspected first-episode deep vein thrombosis who were referred by their physicians to the noninvasive vascular laboratory of University Hospital or Veterans Affairs Medical Center in Oklahoma City, Okla. The patient eligibility criteria were described in detail previously.3 The study protocol is shown in the Figure. Each patient was seen by a consultant physician who performed a clinical assessment. Compression ultrasonography was performed immediately after the clinical assessment. The simplified compression technique was used1 and modified as described below. A scanner (Acuson 128; Acuson Corp., Mountain View, Calif) equipped with a 7.5-MHz linear-array transducer was used. Both the common femoral and popliteal veins were imaged in gray scale and assessed for compressibility in the transverse plane only. The common femoral vein was imaged from the inguinal line to its bifurcation into the superficial femoral vein and profunda femoris. The popliteal vein was imaged from the proximal popliteal fossa to 10 cm distal from the midpatella. The results of compression ultrasonography were classified as follows: normal, if all imaged venous segments were fully compressible; abnormal, if a noncompressible segment was identified; or inadequate, if the results could not be interpreted. The abnormal results were classified according to the site of noncompressibility: common femoral vein only, popliteal vein only, or both sites. Noncompressibility of the popliteal vein was further classified as distal only (between 5 and 10 cm distal from the midpatella) or within the popliteal fossa.

If the result of compression ultrasonography was normal, anticoagulant therapy was withheld and testing repeated 5 to 7 days later. Anticoagulant therapy was withheld from all patients whose results remained normal (the normal cohort), regardless of their symptoms. If the result of initial or repeated compression ultrasonography was abnormal (the abnormal cohort), venography was performed to confirm the presence and extent of thrombosis. Anticoagulant therapy was given to all patients with abnormal results unless it was contraindicated or the results of venography were negative for deep vein thrombosis. All patients were followed up for 3 months at the clinic or by telephone, as described previously.3 All patients who returned during follow-up with suspected deep vein thrombosis or pulmonary embolism underwent objective testing, as described previously,3 according to published protocols and diagnostic criteria.10-14

METHODOLOGIC ISSUES AND AVOIDANCE OF BIAS

Positive predictive value refers to the proportion of patients with abnormal results of compression ultrasonography in whom deep vein thrombosis was present. Venography was used as the reference standard for the presence of deep vein thrombosis.14 The criterion for deep vein thrombosis was an intraluminal filling defect that was constant on all films.14 The positive predictive value for abnormal results of compression ultrasonography was calculated by dividing the number of patients in whom deep vein thrombosis was confirmed by the results of venography (ie, true-positive results) by the number of patients in whom adequate venograms were obtained (ie, the true-positive results plus the false-positive results).

Negative predictive value was defined as the proportion of patients with normal results of compression ultrasonography in whom symptomatic venous thromboembolism during the 3-month follow-up was absent. Care was taken to avoid bias using strategies described previously.1 The results of ultrasonography were interpreted by an expert physician (B.G.B. or T.L.W.) without knowledge of the venography results (if venography was performed). All venograms were interpreted independently by 2 readers without knowledge of the site and extent of the abnormal results of ultrasonography; disagreements were resolved through independent adjudication by a third reader.

STATISTICAL ANALYSIS

The Fisher exact test was used to compare the positive predictive values of abnormal results of ultrasonography of the common femoral vein only, the popliteal vein only, or both sites and to compare the incidences of venous thromboembolism during follow-up between the normal and abnormal cohorts. The 93% confidence intervals (CIs) were calculated from the binomial distribution.

RESULTS

PATIENTS

Of 756 consecutive patients, 716 patients (95%) were eligible; 709 (99%) of these patients gave informed consent to participate. The clinical characteristics of the 709 patients at study entry are shown in Table 1.

COMPRESSION ULTRASONOGRAPHY

The results of compression ultrasonography at presentation were abnormal in 95 patients (13%) and normal in 614 patients (87%). Repeated testing was completed in 521 (85%) of the 614 patients and yielded abnormal results in 9 patients. Thus, the abnormal cohort comprised 104 patients (15%), and the normal cohort, 605 patients (85%).

VENOGRAPHY

Venography was performed in 58 (56%) of the 104 patients in the normal cohort. The reasons for not performing venography were a contraindication (10 patients), above-knee amputation (2 patients), the patient's inability to cooperate (11 patients), inability to obtain intravenous access (7 patients), the patient's refusal (13 patients), and the referring physician's refusal (3 patients). Table 2 shows the venography results and the positive predictive value of ultrasonography according to the site of noncompressibility.
The clinical characteristics of these patients are shown in Table 1. Of the 15 patients with noncompressibility isolated to the common femoral vein, 8 (53%) had pelvic disease documented by computed tomography, magnetic resonance imaging, and/or surgery compared with 2 (5%) of 42 patients with noncompressibility of the popliteal vein only, and 6 (13%) of 47 patients with noncompressibility of both sites ($P<.001$). The conditions in the 8 patients were malignancy in 5 patients (prostate in 1, cervix in 2, renal cell in 1, and lymphoma in 1), benign but progressive neoplasm in 2 patients (teratoma and pelvic lipomatosis), and an extensive abscess in the pelvis and thigh in the remaining patient. The results of venography and/or the findings on pelvic imaging changed management in 8 of the 15 patients.

Six patients had adequate venograms (Table 2). Of the 5 patients in whom deep vein thrombosis was excluded by the results of venography, 3 had extrinsic compression (iliac vein in 2 and vena cava in 1). One patient had a turgid, swollen upper thigh and inguinal region due to a deep abscess. The remaining patient had superficial vein thrombosis that appeared on the results of ultrasonography as a focal 8-mm segment of noncompressibility at the saphenous-femoral junction. The one patient with deep vein thrombosis confirmed by the results of venography had a teratoma compressing the iliac vein.

Five patients had inadequate venograms (Table 2). Extrinsic compression causing inadequate visualization of the deep veins was documented in 3 of the 5 patients (1 patient had pelvic lipomatosis on computed tomographic scans, and 2 patients had recent femoral artery catheterization with large local hematomas). One patient had abrupt termination of the common femoral vein associated with extensive pelvic collateral veins. The fifth patient had superficial vein thrombosis, which appeared as focal noncompressibility at the saphenous-femoral junction on the results of compression ultrasonography.

VENOUS THROMBOEMBOLISM DURING FOLLOW-UP

Of the 709 patients, 708 were successfully followed up for 3 months. One patient, who was homeless, was seen in the clinic 8 weeks after the initial visit and documented to be free of thromboembolic events; this patient was lost to further follow-up. None of the 605 patients in the normal cohort died of pulmonary embolism.

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**Table 1. Clinical Characteristics of the Patients**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All Patients (N = 709)</th>
<th>Normal (N = 605)</th>
<th>Abnormal PV and CFV (N = 47)</th>
<th>Abnormal PV Only (N = 42)</th>
<th>Abnormal CFV Only (N = 15)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (range), y</td>
<td>52.6 (19-98)</td>
<td>51.8 (19-92)</td>
<td>60.6 (31-89)</td>
<td>54.4 (26-98)</td>
<td>55.1 (23-85)</td>
</tr>
<tr>
<td>Men</td>
<td>287 (40)</td>
<td>243 (40)</td>
<td>20 (43)</td>
<td>19 (45)</td>
<td>5 (33)</td>
</tr>
<tr>
<td>Women</td>
<td>422 (60)</td>
<td>362 (60)</td>
<td>27 (57)</td>
<td>23 (55)</td>
<td>10 (67)</td>
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<tr>
<td>Symptoms at Presentation</td>
<td></td>
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<tr>
<td>Pain</td>
<td>567 (80)</td>
<td>489 (81)</td>
<td>38 (81)</td>
<td>30 (71)</td>
<td>10 (67)</td>
</tr>
<tr>
<td>Tenderness</td>
<td>559 (79)</td>
<td>476 (79)</td>
<td>40 (85)</td>
<td>31 (74)</td>
<td>12 (80)</td>
</tr>
<tr>
<td>Swelling</td>
<td>631 (89)</td>
<td>529 (87)</td>
<td>46 (98)</td>
<td>41 (98)</td>
<td>15 (100)</td>
</tr>
<tr>
<td>Pain, tenderness, or swelling</td>
<td>709 (100)</td>
<td>605 (100)</td>
<td>47 (100)</td>
<td>42 (100)</td>
<td>15 (100)</td>
</tr>
<tr>
<td>Median time since symptoms began (range), d</td>
<td>7 (1-365)</td>
<td>8 (1-365)</td>
<td>6 (1-30)</td>
<td>7 (1-28)</td>
<td>7 (1-49)</td>
</tr>
</tbody>
</table>

**Clinical Conditions**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Normal (N = 605)</th>
<th>Abnormal (N = 47)</th>
<th>Abnormal PV Only (N = 42)</th>
<th>Abnormal CFV Only (N = 15)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospitalized in past 6 mo</td>
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<tr>
<td>Surgery in past 6 mo</td>
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<tr>
<td>Cancer</td>
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<td>Congestive heart failure</td>
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<tr>
<td>Immobilized in past month</td>
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<tr>
<td>Postpartum period</td>
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<tr>
<td>Family history of venous thromboembolism</td>
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<td></td>
<td></td>
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<tr>
<td>Superficial phlebitis</td>
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*Data are presented as the number (percentage) of patients unless indicated otherwise. PV indicates popliteal vein; CFV, common femoral vein.*

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(95% CI, 0.0%-0.6%). Four patients (0.7%) in the normal cohort returned with symptomatic venous thromboembolism (95% CI, 0.2%-1.7%) compared with 7 (6.7%) of the 104 patients in the abnormal cohort (95% CI, 2.8%-13.4%; P = .009). Thus, the negative predictive value was 99.3% (601 of 605 patients; 95% CI, 98.3%-99.8%).

### COMMENT

The results suggest 4 inferences. First, noncompressibility isolated to the common femoral vein site has a decreased positive predictive value for deep vein thrombosis. The positive predictive value was only 16.7% for noncompressibility isolated to this site compared with 94.4% for noncompressibility of both sites (see Table 2). Our observed positive predictive value for noncompressibility of both sites is consistent with those of other studies.3,4,6

The lower positive predictive value for isolated noncompressibility of the common femoral vein is unlikely to be due to bias in performing or interpreting venograms. Even if the patients in whom venography was not done or in whom the results were inadequate are counted as having deep vein thrombosis, the positive predictive value is only 67% (10 of 15 patients). This predictive value is too low to be used alone as the diagnostic end point for giving anticoagulant therapy.

The results of venography were inadequate in 5 (45%) of the 11 patients with isolated noncompressibility of the common femoral vein. In contrast, the results in only 6 (13%) of the remaining 47 patients who underwent venography showed inadequate visualization of the deep veins (see Table 2). All venograms and ultrasonography results were interpreted without knowledge of each other or the patient's clinical findings. The higher rate of inadequate venograms among patients with isolated noncompressibility of the common femoral vein is due not to bias but to the underlying disease in these patients, which causes impaired visualization of the deep veins.

Second, noncompressibility isolated to the common femoral vein is a diagnostic marker for important pelvic disease. Of the 15 patients with this finding, 8 had neoplasm or abscess.

Third, for the above reasons, further testing is indicated in patients with noncompressibility isolated to the common femoral vein. The addition of Doppler flow or color flow imaging is unlikely to be helpful since abnormal flow may result from the same pathologic problem causing noncompressibility, and the finding of normal flow does not exclude the presence of nonocclusive thrombosis. Venography has a practical limitation in these patients due to the high rate of inadequate visualization. Magnetic resonance imaging may be useful because it is promising for detecting pelvic and thigh vein thrombosis15-17 and simultaneously provides diagnostic information on other pathologic characteristics in the pelvis.

Fourth, the outcome in the normal cohort supports and extends our earlier results1 and those of Cogo et al.4 Both further testing and anticoagulant treatment can be safely withheld from patients with normal results of compression ultrasonography at presentation and on a single repeated test 5 to 7 days later.

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Reprints: Gary Raskob, PhD, Departments of Medicine and Biostatistics and Epidemiology, University of Oklahoma Health Sciences Center, PO Box 26901, Oklahoma City, OK 73190.

### REFERENCES


