Sensitivity and Specificity of Ultrasonography in the Diagnosis of Upper Extremity Deep Vein Thrombosis

A Systematic Review

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Objectives: To determine the sensitivity and specificity of ultrasonography in the diagnosis of upper extremity deep vein thrombosis and to determine the safety of withholding anticoagulant therapy in patients with negative ultrasonographic results.

Data Sources: The MEDLINE database was searched for literature published from January 1, 1980, to December 31, 2000, that evaluated ultrasonography for the diagnosis of upper extremity deep vein thrombosis. Bibliographies of the retrieved articles were cross-checked to identify additional studies.

Study Selection: All prospective English-language studies were selected. Retrospective studies, review articles, and case reports were excluded.

Data Extraction: Two of us (B.O.M. and S.W.R.) used predefined criteria to independently assess each study.

Data Synthesis: Only one study met all of the predefined criteria for adequately evaluating sensitivity and specificity. The sensitivity of duplex ultrasonography ranged from 56% to 100%, and the specificity ranged from 94% to 100%. No study evaluated the safety of withholding anticoagulant therapy without additional testing in patients with negative ultrasonographic results.

Conclusion: The safety of withholding anticoagulant treatment in a patient with suspected upper extremity deep vein thrombosis and negative ultrasonographic results is uncertain.

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Upper extremity deep vein thrombosis is an increasingly common clinical problem. It may cause pulmonary embolisms, including fatal embolisms. Therefore, accurate diagnosis is essential.

The clinical diagnosis of upper extremity deep vein thrombosis is nonspecific. Its prevalence is less than 50% among symptomatic patients, necessitating objective testing to confirm or exclude the diagnosis. While venography remains the diagnostic reference standard, it is invasive, has an associated risk of thrombophlebitis, and may be unavailable or impractical. Ultrasonography is the most frequently used objective test. However, in contrast to patients with suspected deep vein thrombosis of the legs, the validity of ultrasonographic testing for suspected upper extremity deep vein thrombosis is uncertain. Anatomical differences between the upper and lower extremity deep venous system may influence the performance characteristics of ultrasonography for the diagnosis of upper extremity deep vein thrombosis. For example, the ability to image and compress the middle of the subclavian vein is hindered by the overlying segment of the clavicle. Moreover, which vessels are imaged and the diagnostic criteria for the presence or absence of deep vein thrombosis vary. Most commonly, the subclavian and axillary veins are imaged, but ultrasonographic testing for upper extremity deep vein thrombosis may also include imaging of the internal jugular, innominate, brachial, and basilic veins.

Real-time ultrasonography is used to assess the presence or absence of vein compressibility and the echogenicity within the vein lumen. Doppler ultrasonography evaluates the characteristics of venous flow, including phasicity, pulsatility, and variation with physiologic maneuvers. Duplex ultrasonography uses combined real-time imaging and Doppler ultrasonographic assessment. Color flow Doppler imaging enables the assessment of the presence and direction of venous flow.
Because of the uncertain validity of ultrasonography for the diagnosis of upper extremity deep vein thrombosis, we conducted a systematic review of the literature. Our review had 2 objectives: (1) to determine the sensitivity and specificity of ultrasonography in the diagnosis of upper extremity deep vein thrombosis and (2) to determine the safety of withholding anticoagulant therapy without further objective testing in patients with suspected upper extremity deep vein thrombosis and negative results by ultrasonography.

## MATERIALS AND METHODS

### LITERATURE SEARCH AND DATA SOURCES

The MEDLINE database was searched for literature published from January 1, 1980, through December 31, 2000. Before 1980, no study that used noninvasive vascular imaging for the diagnosis of upper extremity deep vein thrombosis was identified. The Medical Subject Headings’ terms upper extremity and thrombosis were used in separate searches, and studies found during each search were combined. Limits were set for human only and English language only. We supplemented this reference list by cross-checking bibliographies of retrieved articles to identify additional studies.

### STUDY SELECTION AND DATA EXTRACTION

Before performing the literature review, we defined criteria for the inclusion of studies and for assessing the validity of these studies.9,10 We decided a priori to include all prospective studies identified by the literature search, including abstracts, that included ultrasonographic assessment of the upper extremity veins by one or more of the following techniques: real-time ultrasonographic imaging, standard Doppler evaluation, or color flow Doppler imaging. Retrospective studies, review articles, and case reports were excluded. Two of us (B.O.M. and S.W.R.) reviewed each article or abstract independently using the criteria given in Table 1. These criteria were established a priori before the articles were re-

### Table 1. Criteria Used to Review the Studies

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Questions Used to Assess Studies That Evaluated the Sensitivity and Specificity of Ultrasonography in the Diagnosis of Upper Extremity Deep Vein Thrombosis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Does the study include consecutive patients with suspected upper extremity deep vein thrombosis?</td>
</tr>
<tr>
<td></td>
<td>What methods of ultrasonography were used and which vessels were imaged?</td>
</tr>
<tr>
<td></td>
<td>Do all patients undergo ultrasonography and the reference standard, venography?</td>
</tr>
<tr>
<td></td>
<td>Was the venogram interpreted without knowledge of the ultrasonographic results and vice versa?</td>
</tr>
<tr>
<td></td>
<td>Does the study include a broad spectrum of patients (patients with and without upper extremity deep vein thrombosis) and a broad spectrum of patient characteristics (eg, age, sex, and comorbid conditions)?</td>
</tr>
<tr>
<td></td>
<td>What are the reported sensitivity and specificity?</td>
</tr>
<tr>
<td></td>
<td>What are the 95% confidence intervals for the sensitivity and specificity?</td>
</tr>
</tbody>
</table>

<table>
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<tr>
<th>Questions Used to Assess Studies That Evaluated the Safety of Withholding Anticoagulant Therapy Based on Negative Ultrasonographic Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Did all patients with negative ultrasonographic results have their anticoagulation therapy withdrawn or withheld?</td>
</tr>
<tr>
<td>What is the follow-up period (0, &lt;3, 3-6, or &gt;6 mo)?</td>
</tr>
<tr>
<td>What were the outcomes of the follow-up (death, a fatal or symptomatic pulmonary embolism, or symptomatic upper extremity deep vein thrombosis)?</td>
</tr>
</tbody>
</table>

### Table 2. Prospective Studies Evaluating the Use of Ultrasonography in the Diagnosis of Suspected Upper Extremity Deep Vein Thrombosis

<table>
<thead>
<tr>
<th>Patients</th>
<th>Total</th>
<th>Consecutive</th>
<th>Ultrasonographic Technique</th>
<th>Veins Imagined</th>
<th>Interpretation</th>
<th>Broad Spectrum</th>
<th>Patients With Catheter-Related Thrombosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weissleder et al,15 1987</td>
<td>2</td>
<td>2</td>
<td>No</td>
<td>Duplex</td>
<td>Infraglular and subclavian</td>
<td>NI</td>
<td>No</td>
</tr>
<tr>
<td>Falk and Smith,16 1987</td>
<td>22</td>
<td>14</td>
<td>No</td>
<td>Duplex</td>
<td>Infraglular, innominate, subclavian, and axillary</td>
<td>Yes</td>
<td>NI</td>
</tr>
<tr>
<td>Hubsch et al,17 1988</td>
<td>26</td>
<td>9</td>
<td>No</td>
<td>Duplex plus color flow</td>
<td>Subclavian</td>
<td>No</td>
<td>26</td>
</tr>
<tr>
<td>Haire et al,18 1991</td>
<td>43</td>
<td>43</td>
<td>No</td>
<td>Duplex</td>
<td>Infraglular, innominate, subclavian, and axillary</td>
<td>Yes</td>
<td>NI</td>
</tr>
<tr>
<td>Baxter et al,19 1991</td>
<td>19</td>
<td>19</td>
<td>No</td>
<td>Duplex</td>
<td>Subclavian</td>
<td>Yes</td>
<td>14</td>
</tr>
<tr>
<td>Prandoni et al,6 1997</td>
<td>58</td>
<td>58</td>
<td>Yes</td>
<td>Duplex</td>
<td>Infraglular, innominate, subclavian, and axillary</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

*NI indicates data not indicated; NA, data not applicable.†Data are given as percentage (number/total) [95% confidence interval].
viewed according to established methodologic standards for the evaluation of diagnostic tests. A third independent reviewer (T.L.W.) adjudicated disagreements.

**RESULTS**

**LITERATURE SEARCH AND DATA SOURCES**

The literature search identified 18 articles, 6 case reports, and 1 abstract. Of the 18 articles, 12 were excluded: 9 were retrospective studies (a list is available from the authors), 1 included only patients with neck swelling or palpable masses and jugular vein thrombosis,12 1 examined only asymptomatic patients,13 and 1 did not use ultrasonography in the initial diagnosis.14 The 6 case reports were excluded (a list is available from the authors). The one abstract was excluded because of insufficient information to assess study validity. Thus, 6 original prospective studies6,15-19 were assessed using the criteria given in Table 1 and were included in the systematic review.

**STUDY APPRAISAL**

Table 2 summarizes the results of our appraisal of the 6 prospective studies. Only 1 study6 stated that a consecutive series of all patients with suspected upper extremity deep vein thrombosis was examined. All 6 studies6,15-19 included information on the vessels that were imaged and the ultrasonographic methods used. In 4 studies,6,16,18,19 the results of ultrasonography and venography were interpreted independently. Only 1 study6 included enough information to assess the spectrum of patients examined. All studies reported the number of patients in whom thrombosis was associated with a venous catheter. The sample sizes of these studies ranged from 2 to 58 patients (Table 2).

**SENSITIVITY AND SPECIFICITY**

Five studies reported the sensitivity and 3 studies reported the specificity or provided enough information to calculate these values. The sensitivity of ultrasonography ranged from 56% to 100%, and the specificity ranged from 77% to 100%. The sensitivity and specificity varied with the ultrasonographic method used (Table 2). Only 1 study6 reported the 95% confidence intervals for the sensitivity and specificity. The 95% confidence intervals for sensitivity and specificity were calculated for the remaining studies where possible.

**SAFETY OF WITHHOLDING ANTICOAGULANT THERAPY**

No prospective study was identified in which anticoagulant therapy was withheld without additional testing in patients with suspected upper extremity deep vein thrombosis and negative results on ultrasonographic testing. One study6 followed up patients who had undergone ultrasonography and venography; in this study, the decision to give or withhold anticoagulant therapy was based on the venographic results.

**COMMENT**

We sought to determine the sensitivity and specificity of ultrasonography for the diagnosis of upper extremity deep vein thrombosis and to determine the safety of withholding anticoagulant therapy in patients with negative ultrasonographic results. Our results support 3 inferences.

First, only 1 study6 met all of the predefined methodologic criteria11 for adequately evaluating the sensitivity and specificity of a diagnostic test. However, even in this study, the 95% confidence intervals for sensitivity and specificity were broad, indicating that the true sensitivity of duplex ultrasonography could be as low as 82% and that the true specificity could be as low as 69% (Table 2). The remaining studies15-19 lacked details regarding the characteristics of the patients and an independent interpretation of ultrasonography and venography.

Second, there was a clinically important variation (56%-100%) in the sensitivity of ultrasonography for upper extremity deep vein thrombosis (Table 2). This variation is likely due to differences in patient selection and the ultrasonographic technique used and the relatively few patients examined in all studies. The main limitation of real-time imaging of the upper extremity is imaging the portion of the subclavian vein that passes beneath the clavicle. Haire et al6 found that this was the major cause of poor sensitivity and that it occurred most often on the left side. The specificity of duplex ultrasonography was high (94%-100%) (Table 2).

The sensitivity and specificity of ultrasonography varied with the technique used. The results indicate that Doppler evaluation alone is less sensitive and less specific than real-time imaging or duplex ultrasonography for upper extremity deep vein thrombosis.6 The available data do not support an important improvement in sensitivity and specificity by the addition of color flow Doppler imaging over real-time imaging alone.

Third, no study has evaluated the safety of withholding anticoagulant therapy without additional testing in patients with suspected upper extremity deep vein thrombosis.6 The available data do not support an important improvement in sensitivity and specificity by the addition of color flow Doppler imaging over real-time imaging alone.

We conclude that ultrasonography for clinically suspected upper extremity deep vein thrombosis has not been adequately evaluated. The safety of withholding anticoagulant treatment in a patient with suspected upper extremity deep vein thrombosis and negative ultrasonographic results is uncertain. There is a need for prospective studies in more patients using the design features outlined in...
Table 1 to definitively evaluate the sensitivity, specificity, and safety of duplex ultrasonography for the diagnosis of upper extremity deep vein thrombosis.

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REFERENCES


