The Characteristics of the Thrombi of the Lower Limbs, as Detected by Ultrasonic Scanning, Do Not Predict Pulmonary Embolism*

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**Objective:** To evaluate whether pulmonary embolism (PE), as detected by perfusion lung scan, could be predicted by the ultrasonic (US) characteristics of the thrombi in patients with deep venous thrombosis (DVT) of the lower limbs.

**Patients:** Ninety-three consecutive patients with DVT and no symptoms of lung involvement (52 men, 41 women; mean age, 67±17 years).

**Measurements and results:** The degree of thrombotic involvement of the lower limbs was assessed using a US score system ranging from 1 (indicating a subsegmental, nonocclusive thrombus) to 16 (massive, occlusive). According to the echographic and color-Doppler features, the thrombi were classified in terms of echorereflectivity, adhesiveness to the vein wall, and organization. The diagnosis of PE (PIOPED criteria) was highly probable in 46% of the patients, intermediate in 15%, low in 8%, and very low/normal in 31%. No correlations were found between the lung scan findings on one side and the venous scoring system or the US features of the thrombi on the other side.

**Conclusions:** While confirming that the prevalence of PE in patients with DVT is elevated, we failed to define a subgroup of patients at higher risk. Our data imply that lung scan should be used extensively for the detection of silent PE and that anticoagulation should not be graded on US findings.

**Key words:** color Doppler; deep venous thrombosis; lung scan; pulmonary embolism

**Abbreviations:** aPTT=activated partial thromboplastin time; CXR=chest radiograph; DVT=deep venous thrombosis; PE=pulmonary embolism; PIOPED=Prospective Investigation of Pulmonary Embolism Diagnosis; US=ultrasonic scanning

Several studies have shown a high prevalence of pulmonary embolism (PE), as detected by scintigraphic scanning, in patients affected by deep venous thrombosis (DVT) of the lower limbs, even when clinical signs and/or symptoms of lung involvement are lacking.1-10

Ultrasonic scanning (US) is now accepted as the first line of investigation for the diagnosis of proximal DVT (that is, the thrombosis involving the thigh and the popliteal vein, which is associated with a particularly high embolic risk), being both sensitive and specific, for comparison with contrast venography.11-21 In fact, apart from its diagnostic power, US allows us to estimate the extension of a thrombus and to appreciate relevant characteristics, such as its adhesion to the venous wall and its age.22-25

The aim of the present study was to verify whether the presence of perfusion defects at lung scan in patients with DVT could be related to the characteristics of the thrombus in the lower limbs, as detected by US.

**Materials and Methods**

In our center for the diagnosis and treatment of DVT, accredited by the European Working Group on Vascular Medicine of the International Union of Angiology as Teaching Centre, we consecutively investigated a total number of 93 patients with proximal DVT, from June 1993 to June 1995. No one had signs or symptoms of PE, when first seen. Fifty-two were male, and 41 were female. The mean age (±SD) was 67±17 years, with a range from 21 to 95 years. The DVT was primary in 35, and secondary to predisposing conditions in the remaining 58. We considered as secondary thrombotic events that occurred after major surgery requiring more than 3 h general anesthesia (15 patients), major trauma or trauma to the lower limbs (15 patients), extensive or metastatic malignancy (16 patients), prolonged immobilization due to severe heart failure or paraplegia (11 patients), and antithrombin III deficiency (1 patient). In 13 patients, the DVT was bilateral.

**Ultrasonic Scanning**

The diagnosis of DVT was made through a commercial color-flow imaging ultrasonic instrumentation, with probes of 5 and 7.5 MHz,
following a standardized procedure. In brief, each patient was examined in a standing position, and the deep veins were visualized from the groin to the popliteal fossa. The detection of a thrombus was based on the finding of a noncompressible vein segment, by pushing the hand-held probe over the vein itself. The absence of spontaneous or provoked venous Doppler signal (color-coded) and the direct visualization of a thrombus (fixed echo-reflective material within the vein lumen) were adjunctive criteria.

For quantification purposes, following the recommendations of the Committee on Reporting Standards in Venous Disease, veins were divided into four segments, namely the following: iliac-common femoral, superficial femoral, popliteal, and below knee. The degree of involvement of each segment was defined through a score system, as follows: 0=normal; 1=subsegmental (less than a whole segment), nonocclusive; 2=subsegmental, occlusive; 3=segmental, nonocclusive; and 4=segmental, occlusive. Thus, with this system, the total score of a single limb could go from 0 (ie, normalcy) to a maximum of 16 (ie, massive, totally occlusive involvement), reflecting the extension of the process.

The presence of a floating head in the most proximal portion of a thrombus was carefully looked for systematically in each case; moreover, based on the real-time flow-imaging system, the persistence of a peripheral residual lumen separating the thrombus from the vein wall somewhere along its body (made evident by provoking flow acceleration manually, compressing the leg distally to the site under visualization) also was searched for. Altogether, these two aspects were considered as indicating incomplete adherence of the thrombus, early age, and potential risk for detachment and embolism. The evidence of flow within a thrombus provoked by compressive maneuvers (as above) was considered as indicating organization and, along with echoreflectivity, aged thrombus; a thrombus with such characteristics was regarded as deprived of embolic potential.

### Table 1—Cross Tabulation of the Distribution of the Diagnosis of Pulmonary Embolism (PIOPED Criteria) and the Extension of Lower Limbs Venous Thrombosis*

<table>
<thead>
<tr>
<th>PE Probability (PIOPED Criteria)</th>
<th>&lt;4</th>
<th>5-8</th>
<th>9-12</th>
<th>&gt;12</th>
<th>Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very low/normal</td>
<td>8</td>
<td>13</td>
<td>7</td>
<td>29</td>
<td>(31)</td>
</tr>
<tr>
<td>Low</td>
<td>1</td>
<td>0</td>
<td>5</td>
<td>7</td>
<td>(8)</td>
</tr>
<tr>
<td>Intermediate</td>
<td>4</td>
<td>6</td>
<td>3</td>
<td>14</td>
<td>(15)</td>
</tr>
<tr>
<td>High</td>
<td>10</td>
<td>11</td>
<td>19</td>
<td>43</td>
<td>(46)</td>
</tr>
<tr>
<td>Total</td>
<td>23</td>
<td>34</td>
<td>34</td>
<td>93</td>
<td>(100)</td>
</tr>
</tbody>
</table>

*As assessed by a scoring system (see text for details); χ²=11.4; p=0.24.

### Table 2—Distribution of the Diagnosis of PE (PIOPED Criteria), According to the Causes of DVT*

<table>
<thead>
<tr>
<th>Causes of DVT</th>
<th>PE Probability (PIOPED Criteria)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Primary</td>
</tr>
<tr>
<td>Very low/normal (29)</td>
<td>9</td>
</tr>
<tr>
<td>Low (7)</td>
<td>5</td>
</tr>
<tr>
<td>Intermediate (14)</td>
<td>5</td>
</tr>
<tr>
<td>High (43)</td>
<td>17</td>
</tr>
<tr>
<td>Total</td>
<td>36</td>
</tr>
</tbody>
</table>

*The single patient with antithrombin III deficiency (not shown here) had a normal lung scan. No statistically significant differences were observed (χ²=8.06; p=0.089).

### Lung Scan

All patients were submitted to a perfusion lung scan (Q) with 99mTc-labeled macroaggregates of albumin, following standardized procedures (multiple static images of the lungs from six different planar projections), and to a ventilatory lung scan (Q) with a pseudogas made of microrized macroagglomeroids labeled with 99mTc, whenever defects became evident on the previous perfusion scan. All patients were also submitted to a standard chest radiographic examination (CXR). The perfusion scan was completed by 72 h from the US evaluation. The diagnosis of PE was made in the presence of perfusion defects, according to the criteria of the Prospective Investigation of Pulmonary Embolism Diagnosis (PIOPED) Study, as amended by a subsequent revision. In essence, these studies establish four classes of probable diagnosis (namely: high, intermediate, low, very low) with the following requirements: high probability—at least 2 large segmental perfusion defects (>75% of a lung segment) with no (or substantially larger than) associated ventilatory defects, or 1 large and at least 2 medium-sized defects (25 to 75% of a segment), or at least 4 medium-sized defects; intermediate—a single medium sized defect, or defects that fail to fulfill the criteria of the preceding and of the following class; low—more than 3 small-sized (<25% of a segment) defects, or defects substantially smaller than corresponding CXR abnormalities, or nonsegmental perfusion defects, or defects surrounded by normally perfused lung (stripe sign), or multiple matched VQ defects (regardless of size) with normal CXR; very low—3 or less small defects. In practice, very low probability does not support the diagnosis of PE, while low probability means that it is questionable at the best. The positive predictive value of high and intermediate probability scans are 87% and 30%, respectively.

As for the medical treatment, at the time of the lung scan 75 patients were being treated with conventional anticoagulant therapy (IV bolus of 100 U/kg of unfractionated heparin, followed by continuous IV infusion of 1,000 to 1,500 U/h and by warfarin po, under strict control of activated partial thromboplastin time [aPTT] and international normalized ratio); 17 patients were treated with a nonconventional form of anticoagulant therapy (subcutaneous calcium heparin, 12,500 U bid, irrespective of the aPTT). A single patient, already being treated steadily with warfarin po, was kept under the same regimen. In each patient, the treatment had been chosen by the referring physician, independently of the instrumental findings.

The statistical analysis consisted in comparing frequency distribution with χ² testing.

### RESULTS

The median interval between the onset of symptoms in the leg and the US diagnosis of proximal DVT performed in our laboratory was 9 days (range, 0 to 60
days: 7 patients had their conditions diagnosed within 24 h, 36 between day 2-7, 14 between 8-14, 22 between 15-20, and 14 between 21-60.

The degree of thrombotic involvement of the lower limbs, as assessed by the scoring system, was below 4 in 6 patients (6%), 5 to 8 in 23 (25%), 9 to 12 in 30 (32%), and above 12 in 34 (36%). The lung scan allowed a diagnosis of PE with high probability in 43 patients (46%), intermediate probability in 14 (15%), low probability in 7 (8%), and very low (virtually normal) in 29 (31%). No correlation was found between the venous scoring system and the lung scan findings (Table 1), although a positive trend toward an increased frequency of high-probability lung scan in patients with higher US score was observed. Likewise, no correlation was found between the lung scan categories and the clinical setting; specifically, the patients with primary thrombosis did not differ from those with secondary thrombosis (Table 2).

As for the echographic characteristics of thrombi, 22 (27%) were incompletely adhesive, 42 (45%) were nonechoreffective, and 45 (48%) were nonorganized. No correlation was found between these parameters considered individually (Table 3) or in combination (Table 4) and the lung scan findings.

As for treatment, the patients with conventional anticoagulant therapy (75) showed the same proportion of abnormal lung scan as the others (18 patients treated with uniform doses of subcutaneous heparin or with warfarin) (Table 5).

During hospitalization, 2 patients died of PE and 15 developed compatible (albeit light) symptoms, such as dyspnea (10), fatigue (4), and thoracic pain (1). In this subgroup, the lung scan was high probability in 14 and intermediate in 1.

**DISCUSSION**

The evidence that a proximal venous thrombosis of the lower limbs is often associated with PE is substantial.\(^1\)\(^-\)\(^10\) Despite the fact that it remains clinically silent in most cases, PE is regarded as an ominous event, being one of the most important causes of in-hospital mortality in many clinical settings.\(^2\)\(^9\),\(^3\)\(^0\) The employment of objective and reproducible diagnostic tests is very important to precisely quantify and predict such a risk. In this respect, \(^99m\)Tc-labeled macroaggregates of albumin scintigraphy and venous ultrasonic examination are accepted as adequate tools, being noninvasive, sensitive, and specific. As for scintigraphy, the PIOPED criteria are well-defined in terms of sensitivity, specificity, and predictive value, and have been employed largely since their publication.\(^2\)\(^7\),\(^2\)\(^8\)

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### Table 3—Distribution of the Diagnosis of PE According to the Different Echographic Characteristics of the Venous Thrombi*

<table>
<thead>
<tr>
<th>US Characteristics of DVT</th>
<th>Vein Wall Adhesion</th>
<th>Echoreflectivity</th>
<th>Organization</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Very low/normal (29)</td>
<td>24</td>
<td>20</td>
<td>18</td>
</tr>
<tr>
<td>Low (7)</td>
<td>5</td>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td>Intermediate (14)</td>
<td>2</td>
<td>10</td>
<td>4</td>
</tr>
<tr>
<td>High (43)</td>
<td>10</td>
<td>25</td>
<td>22</td>
</tr>
<tr>
<td>Total</td>
<td>39</td>
<td>74</td>
<td>34</td>
</tr>
</tbody>
</table>

*No statistically significant differences were observed. Complete adhesion to the vein wall: \(\chi^2 = 3.61; p = 0.414\); echoreflectivity: \(\chi^2 = 6.61; p = 0.115\); organization: \(\chi^2 = 8.16; p = 0.055\).

### Table 4—Distribution of the Diagnosis of PE According to the Presence of Different Echographic Characteristics of the Venous Thrombi Considered as Risk Factors (Incomplete Adhesion to the Vein Wall, Lack of Echoreflectivity, Lack of Organization)*

<table>
<thead>
<tr>
<th>PE Probability (PIOPED Criteria)</th>
<th>US Characteristics of DVT</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>≤1</td>
</tr>
<tr>
<td>Very low/normal (29)</td>
<td>13</td>
</tr>
<tr>
<td>Low (7)</td>
<td>4</td>
</tr>
<tr>
<td>Intermediate (14)</td>
<td>6</td>
</tr>
<tr>
<td>High (43)</td>
<td>11</td>
</tr>
<tr>
<td>Total</td>
<td>34</td>
</tr>
</tbody>
</table>

*No statistically significant differences were observed (\(\chi^2 = 6.03; p = 0.420\)).
In our set of consecutive DVT patients, a perfusion lung scan was systematically planned within 3 days from the diagnosis, excluding those in whom a PE could be suspected from the beginning. We observed a prevalence of 46% of high-probability and 15% of intermediate-probability lung scan, for an estimated 45% of true-positive cases (considering a positive predictive value of 87% and 30% for each category, respectively). This figure may well be an underestimate, due to the low sensitivity of the scintigraphic method; moreover, in our study, the US diagnosis of DVT occurred several days after its onset (median, 9 days), and, consequently, we might have missed early recovered PE. The prevalence of silent PE reported in the literature spans over a wide range, from 22 to 59%, reflecting the fact that not all researchers adopted the same scintigraphic criteria and that the selection of the patients and the timing of scintigraphy differed from one study to another.

To verify whether PE could be predicted by the ultrasonic characteristics of the venous thrombi in the legs, we categorized thrombi according to their extension, adhesion to the vein wall, organization, and echorectivity. We assumed that an extensive thrombus, with a floating head (which is rarely seen) or not completely adherent to the wall, uniformly hyperechoic is at maximal risk for embolism, but it must be underlined that the validity of this assumption has not been demonstrated yet (to our knowledge), mainly because comparison studies in vivo are lacking.

We failed to observe any predictive feature. In fact, the prevalence of abnormal lung scan was not higher in patients with increasingly extensive thrombosis, nor in those whose thrombus was not completely adherent to the wall and/or relatively fresh (nonchorespective, nonorganized) (Tables 3 and 4). Furthermore, no echographic feature (nor any combination of features) was associated with an increased risk of high-probability lung scan. To the best of our knowledge, no other comparison studies of this kind have been reported in the literature.

The interpretation of these results is not clearcut, reflecting our poor comprehension of the natural evolution of venous thrombi and pulmonary perfusion defects. For example, we do not know exactly the evolution of thrombi during time and the time course of changing. Similarly, we do not know how long it takes for a perfusion defect in the lungs to disappear.

In a way, it might not be surprising to find no relationship between the severity of a DVT and the occurrence of PE; paradoxically, we might even expect an inverse correlation, because a circumscribed (ie, subsegmentary, nonocclusive) thrombosis might be the result of a major embolus from a previous extended (ie, segmentary, occlusive) thrombosis.

Likewise, the type of treatment did not seem to affect the incidence of PE. In fact, the prevalence of PE in patients treated with fixed doses of heparin and in those treated with adjusted doses was similar. In the former patients, the aPTT was not monitored, so we do not know whether the actual intensity of medication was adequate; however, in general, they received less heparin on a daily basis than conventionally treated ones. These patients were not selected because of a less extensively involved disease (or suspected so); indeed, the reason for their putative undertreatment was a more cautious attitude of their physician in relation to potential hemorrhages. While it remains controversial which daily dose of heparin is most beneficial in DVT patients, it does not seem to be surprising that minor embolism (mostly asymptomatic) is not prevented by anticoagulant therapy, because heparin is not expected to influence an existing thrombus, but to prevent overgrowth and recurrence.

In conclusion, we confirm that the incidence of PE in patients with DVT is high and support the view that, due to the impossibility to identify a subgroup of patients at higher risk, it seems important to keep a high suspicion index in all, and to employ lung scan extensively. We actually recommend that every patient with proximal DVT should undergo a screening lung test. Furthermore, our results imply that an anticoagulant therapy should not be graded on the US findings, and that, once the diagnosis is set, it should be implemented independently of the severity of the venous involvement.

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**Table 5—Distribution of the Diagnosis of PE According to the Type of Therapy (Nonconventional: Fixed Dose of Heparin; Conventional: Adjusted Dose of Heparin)**

<table>
<thead>
<tr>
<th>PE Probability (PIOPED Criteria)</th>
<th>Nonconventional</th>
<th>Conventional</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very low/normal (29)</td>
<td>8</td>
<td>21</td>
</tr>
<tr>
<td>Low (7)</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>Intermediate (14)</td>
<td>3</td>
<td>11</td>
</tr>
<tr>
<td>High (43)</td>
<td>6</td>
<td>37</td>
</tr>
<tr>
<td>Total</td>
<td>18</td>
<td>75</td>
</tr>
</tbody>
</table>

$\chi^2=1.97; p=0.78.$

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References
27 PIOPED Investigators. Value of the ventilation/perfusion scan in acute pulmonary embolism: result of the Prospective Investigation of Pulmonary Embolism Diagnosis (PIOPED). JAMA 1990; 263:2753-59
29 Smith GT, Dammin GJ, Bester L. Postmortem arteriographic studies of the human lung in pulmonary embolization. JAMA 1964; 188:143-48
32 Webber MM, Gomes AS. Comparison of Biello, Menefelt and PIOPED criteria for the diagnosis of pulmonary emboli on lung scans. Am J Radiol 1990; 154:975-81