Detection of Pelvic Vein Thrombosis by Magnetic Resonance Angiography in Patients With Acute Pulmonary Embolism and Normal Lower Limb Compression Ultrasonography*

Jean-Baptiste Stern, MD; Marc Abehsera, MD; Dominique Grenet, MD; Sylvie Friard, MD; Louis-Jean Couderc, MD; Antoine Scherrer, MD; and Marc Stern, MD

Study objective: In patients with proven acute pulmonary embolism (PE), a systematic search for “residual” deep vein thrombosis (DVT) using venography or compression duplex ultrasonography (CDUS) of the lower limbs is negative in 20 to 50% of patients. We hypothesized that undetectable pelvic vein thrombosis (from the external iliac vein to the inferior vena cava) could account for a substantial proportion of patients with negative CDUS findings. Using a noninvasive test, magnetic resonance angiography (MRA), the objective of the study was to assess the prevalence of pelvic DVT in patients with acute PEs and normal findings on lower limb CDUS.

Design: Prospective study.

Setting: A 35-bed respiratory unit in a 680-bed Parisian teaching hospital.

Patients: From June 1995 to October 1996, 24 patients (mean age, 49 years; age range, 18 to 83 years) with acute PEs and normal findings on lower limb CDUS underwent pelvic MRA.

Measurements and results: MRA disclosed pelvic DVT in seven patients (29%). The common iliac vein was involved in five patients. Internal iliac vein (hypogastric) thrombosis was imaged in two patients, but no patients had DVT limited to this vein. Three patients underwent subsequent venography studies that confirmed the MRA findings. In three other patients, a new MRA at the end of anticoagulant therapy showed the resolution of the DVT.

Conclusions: Our data support the view that, among patients with negative findings on CDUS, a substantial proportion of the DVTs that are responsible for PE originates in the pelvic veins. This study provides additional arguments to suggest that MRA might become the reference test for the exploration of pelvic DVT.

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Key words: caval filters; deep vein thrombosis; iliac vein; inferior vena cava; magnetic resonance angiography; pelvic veins thrombosis; pulmonary embolism; thromboembolism; venography

Abbreviations: CDUS = compression duplex ultrasonography; DVT = deep vein thrombosis; LS = lung scan; MRA = magnetic resonance angiography; PE = pulmonary embolism

In the United States, pulmonary embolism (PE) occurs each year in approximately 600,000 patients, leading to 60,000 deaths,1 and in France, fatal PE is estimated at 10,000 to 20,000 cases yearly. Despite advances in clinical diagnosis, a delay in the diagnosis is still the main source of mortality from PE, and an autopsy series2 has indicated that PE remains undiagnosed at death in as many as 40 to 70% of patients.

Since a clear relationship has been established between PE and deep vein thrombosis (DVT), looking for DVT now has been integrated into diagnostic algorithms for patients with suspected PEs.1,3 The prevalence of detectable DVT in patients with confirmed PEs is subject to discrepancies that are due mostly to the procedure employed to diagnose PE and DVT. Compression duplex ultrasonography (CDUS) is a safe tool that is used routinely in patients with suspected venous thromboemboli. Among patients with confirmed PEs, 15 to 50%...
presented with a DVT that was diagnosed by CDUS. The sensitivity decreases in asymptomatic patients and is weak for the detection of pelvic DVT (from the external iliac vein to the inferior vena cava). Contrast venography, a more invasive test, detected DVT in 70 to 80% of patients with confirmed PEs. As for CDUS, the exploration of pelvic veins by venography is imperfect, leading to a focusing of attention on new noninvasive imaging procedures that are available for diagnosing pelvic DVT.

In some studies, magnetic resonance angiography (MRA) has been evaluated for the diagnosis of lower limb DVT. In patients with clinically suspected DVT, MRA seemed to be accurate, showing a 95 to 100% sensitivity and a 50 to 100% specificity for the detection of DVT. Furthermore, in 25 patients with femoro-iliocaval venous thrombosis, MRA demonstrated a 100% sensitivity and a 98.5% specificity compared with contrast venography.

Using MRA, the objective of the study was to assess the prevalence of pelvic DVT in patients with acute PEs and normal findings on lower limb CDUS.

**Materials and Methods**

**Design of the Study**

The study was conducted between June 1995 and October 1996 in a 35-bed respiratory unit, which is part of a 680-bed teaching hospital. Patients with confirmed PEs and normal findings on lower limb CDUS were included, except for patients with contraindications to MRA, patients with hemodynamic instability, and patients in ICUs. All patients enrolled in the study were informed and agreed to participate. They were informed that in case a DVT was found on MRA, iliocaval venography, contrast venography, and MRA were performed. Thrombosis was defined by a constant intraluminal filling defect or abrupt cutoff in a deep vein. No. of excitations, 1; and saturation, inferior to superior.

**Iliocaval Venography**

Iliocaval venography was performed bilaterally by the injection of 120 mL of contrast medium (Hexabrix; Guerbet; Roissy, France) through a bilateral catheter in common femoral veins with the patient in a supine position. Thrombosis was defined as a constant intraluminal filling defect or abrupt cutoff in a deep vein. Nonopacification of a large vein associated with collateral venous circulation was taken as presumptive of the presence of DVT.

**MRA Procedure**

MRA studies were performed in a 1.5-T unit (Signa Horizon; General Electric; Fairfield, CT) that had been acquired in May 1995. The standardized protocol consisted of sequential axial gradient echo images, from the inferior vena cava to the common femoral veins, with two-dimensional time-of-flight venography. The image parameters were as follows: 200-msec echo time; 200-msec repetition time; flip angle, 60°; time of repetition, 45 ms; minimum time of echo; field of view, 36 to 40 cm; slice thickness, 2.9 mm; matrix size, 256 × 128; No. of excitations, 1; and saturation, superior to inferior.

MRA images were reconstructed using the maximum intensity projection. Criteria for the diagnosis of DVT were defined by an intravascular filling defect with low signal intensity surrounded by an area of high signal intensity, corresponding to the residual flowing blood. A complete clot was defined by an absence of signal with or without a collateral vessel.

**Diagnosis of PE**

The diagnostic criteria for PE were those described in the prospective investigation of acute PE diagnosis (the PISA-PED study). The clinical probability of PE was based on an evaluation of the clinical history, a physical examination, a chest radiograph, an ECG, and an arterial blood gas analysis. Based on the clinical probability, patients underwent perfusion lung scans (Ls) only, or associated with pulmonary angiography and/or spiral CT scan. All patients underwent a perfusion LS between day 10 and day 15 after receiving the initial diagnosis of PE.

**Risk Factors for Thromboembolism**

For each patient, the biological and nonbiological thrombophilic states were prospectively screened. The biological thrombophilic state included plasmatic research of antiphospholipid antibody, factor V Leiden mutation (ie, activated protein C resistance), and deficiency of protein C, protein S and antithrombin. Patients were considered to be in a clinical thrombophilic state if they presented with at least one of the following conditions: previous thromboembolism; marked preoperative or postoperative immobility; had undergone surgery for malignant disease; and had undergone estrogen therapy.

**Statistical Analysis**

A Student t test for numerical data or a Fisher Exact Test for categoric data was used to compare the clinical characteristics of patients with and without pelvic DVTs.

**Results**

During the study period, PE was diagnosed in 118 patients. Among these 118 patients, 24 met
the inclusion criteria and underwent a pelvic MRA. These 24 patients constitute the basis of the study (Table 1).

Table 1—Clinical Characteristics of Patients*

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Values (n = 24)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>13</td>
</tr>
<tr>
<td>Female</td>
<td>11</td>
</tr>
<tr>
<td>Age, yr†</td>
<td>49 (18–83)</td>
</tr>
<tr>
<td>Thrombophilic risk‡</td>
<td></td>
</tr>
<tr>
<td>Biological§</td>
<td>8 (33.3)</td>
</tr>
<tr>
<td>Clinical¶</td>
<td>11 (45.8)</td>
</tr>
<tr>
<td>Patients without identified thrombophilic state</td>
<td>9 (37.5)</td>
</tr>
<tr>
<td>PE diagnosis</td>
<td></td>
</tr>
<tr>
<td>Perfusion LS</td>
<td>6 (25)</td>
</tr>
<tr>
<td>Perfusion LS, spiral CT scan</td>
<td>13 (54.6)</td>
</tr>
<tr>
<td>Perfusion LS, spiral CT scan, pulmonary angiography</td>
<td>3 (12.5)</td>
</tr>
<tr>
<td>Perfusion LS, pulmonary angiography</td>
<td>2 (8)</td>
</tr>
</tbody>
</table>

*Values given as No. (%), unless otherwise indicated.
†Values given as mean (range).
‡Some patients combined biological and clinical thromboembolism risk factors.
§Risk: antiphospholipid antibody (n = 2); activated protein C resistance (n = 2); deficiency of protein C (n = 2); deficiency of antithrombin (n = 1); antiphospholipid antibody and deficiency of protein S (n = 1).
¶Risk: marked immobility (n = 4); estrogen therapy (n = 3); previous thromboembolic event (n = 3); and surgery for malignant disease (n = 1).

MRA disclosed pelvic DVTs in 7 patients (29%), and the findings were normal in 17 patients (71%). The topography of the seven pelvic DVTs was the common iliac vein in five patients, either the left (three patients) or the right (two patients). In two of these five patients, an internal iliac DVT was also present (Fig 1). Pelvic DVT involved the inferior vena cava in one patient and the right external iliac vein in the last patient. No isolated internal iliac thrombosis was imaged by MRA.

The seven patients with pelvic DVTs were younger than those without pelvic DVTs found on MRA (mean age, 35 vs 57 years, respectively; p = 0.01). The prevalence of risk factors for venous thromboembolism was not statistically different between patients with or without pelvic DVTs. None of the patients was symptomatic for a lower limb DVT.

In three patients with pelvic DVTs, we had the opportunity to perform an iliocaval venography. There was no discrepancy between the findings of the MRA and those of the iliocaval venography, except for the two internal iliac DVTs, which were not seen on venograms (Fig 1, 2).

Four patients with pelvic DVTs that were found on MRA did not receive venography (interval between MRA and venography was ≥ 48 h, one patient; and contrast allergy, three patients). Three of these patients underwent a second MRA after the completion of 6 months of anticoagulant therapy. A

Figure 1. MRA reconstructed using the maximum intensity projection showing a thrombosis of the right common iliac vein. The thrombosis involves also the inferior vena cava. The left internal iliac vein is clearly shown, whereas the right internal iliac vein is not, suggesting that this vein also had undergone thrombosis. LA = left anterior.
new MRA showed a complete resolution of the previously noted abnormalities, suggesting the regression of the pelvic DVT by treatment (Fig 3, 4).

MRA findings were considered to be normal in 17 patients (71%). Five of these 17 patients had undergone a unilateral iliocavography, which was performed via the femoral route, as the first stage of pulmonary angiography. Iliocavography findings were normal in all cases.

The mean duration of hospital stay was 12.8 days (range, 7 to 25 days) in patients with pelvic DVTs, and 11.1 days (range, 4 to 30 days) in patients without pelvic DVTs ($p = 0.6$).

**Discussion**

This study provides original information focusing on the relationship between PE and DVT and offers interesting perspectives for MRA as a noninvasive procedure for the diagnosis of pelvic DVT. The prevalence of pelvic DVT in 24 patients with proven PEs and normal findings on CDUS was 29%. The common iliac vein was the most frequently involved vein. No patient had isolated internal iliac vein (hypogastric) thrombosis.

MRA has previously been employed in patients with suspected lower limb DVTs, showing an excel-
lent sensitivity (95 to 100%) and a specificity ranging from 80 to 100% compared with venography.\textsuperscript{9,11,12,17} Although all patients with DVTs found on MRA did not undergo contrast venography, MRA and iliocaval venography showed a perfect concordance in the three patients in whom both tests were performed. In a prospective study\textsuperscript{13} comparing MRA and venography for femoro-iliocaval DVT, interobserver dis-

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{image1.png}
\caption{Axial MRA of the same patient as in Figure 3 after 6 months of anticoagulation treatment showing the resolution of the thrombosis.}
\end{figure}
crepancies were noted on only 2 of 200 venous segments analyzed. This variability is lower than that observed with conventional venography for which intraobserver variability is seen in as many as 15% of patients.18

To the best of our knowledge, there has been no previous study using MRA to evaluate the prevalence of DVT in patients with proven PE. Selecting patients with normal CDUS, our study selected a particular sample of patients with PEs (ie, 21% of patients who had experienced PEs over a 16-month period). Thromboses limited to the pelvic veins are uncommon even in patients with proven PEs. Using contrast venography of the lower limbs as a diagnosis test, Girard et al6 have reported an 82% prevalence of detectable DVTs in patients with acute PEs. Even if the upper level of DVTs was the iliac or caval vein for 23% of patients, only four patients (2%) with acute PEs had thrombi that were limited to the iliac vein and/or the inferior vena cava. In our series, we hypothesized that pelvic clots disclosed by the MRA were not extensions of lower limb thrombosis but were really limited to pelvic veins. Indeed, all patients had negative findings on lower limb CDUS, which is highly accurate in diagnosing femoral DVTs, approaching 100% sensitivity in symptomatic patients.10,19 However, CDUS sensitivity decreases in asymptomatic patients,20 and its ability to detect iliac and central venous DVTs is lacking.9,19 Laissy et al10 demonstrated that MRA was more accurate than CDUS in revealing an extension to the pelvis of a lower limb DVT (MRA sensitivity, 95%; CDUS sensitivity, 46%).

This study suggests that, among patients with negative CDUS findings, nearly one third of DVTs that are responsible for PEs originate in the pelvic veins, even in patients without a particularly high risk for pelvic thrombosis. As suggested by other authors,11,21 MRA seems to be the reference test for the exploration of pelvic DVT. One may assert that DVT limited to the internal iliac vein may not be properly detected using contrast venography. Even if none of our 24 patients had thrombi limited to the internal iliac vein, 2 patients had internal iliac DVT imaged by MRA. Internal iliac vein thromboses were not imaged by iliofemoral venography, suggesting that MRA was more sensitive for these deep veins. Internal iliac veins were accurately visualized by MRA in 98% of a 166-patient series.9

Three patients in our study had undergone a new MRA after 6 months of anticoagulant treatment, which showed the complete resolution of the pelvic DVT. As shown by other authors,11,21 MRA can be repeated easily. In our study, the maximum duration of the MRA was 15 min (with the patient staying on the examination table), which is less time than the mean reported durations, ranging from 30 min to 1 h.9,11–13,17 The absence of gadolinium injection, as well as the evolution of the imaging technique over time can account for the shorter duration of the procedure. Newer technologies are likely to provide better images, and it is uncertain how our results can be extrapolated to a new generation MRA scanners. But, to the best of our knowledge, no study on this specific topic (detection of pelvic DVT) has been published so far.

The accuracy of MRA for the exploration of pelvic veins could have direct clinical implications for the management of patients with thromboembolism disease, particularly for the indication of the insertion of inferior vena cava filters. MRA could more accurately detect large proximal or free-floating thrombi, which represent in some circumstances an indication for filter insertion.22 However, one may acknowledge that, in our patients, performing an MRA did not lead either to treatment modification or to an indication for filter insertion. Even if MRA is rarely routinely available, this test could be performed in patients for whom contrast injection or irradiation is dangerous, such as those with renal or cardiac insufficiency, those with allergies, and those who are pregnant.

The place of this procedure in the diagnosis of thromboembolism is still unclear. There is no consensus for its use. The American College of Chest Physicians consensus committee underlined the lack of large studies and considered this test to be "institution specific."23 At a time when noninvasive procedures are largely integrated into diagnosis algorithms,24 MRA fits the criteria for a safe and accurate procedure. The results of a preliminary study demonstrated high sensitivity and specificity of gadolinium-enhanced MRA of pulmonary arteries for the diagnosis of PE.25 This may encourage future studies focusing on the efficiency of MRA as a single-time procedure for the diagnosis of PE and DVT.

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REFERENCES