Performance of magnetic resonance angiography in suspected acute pulmonary embolism

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Summary
Pulmonary embolism (PE) is a common and potentially fatal disorder. Non-specific findings make the clinical diagnosis of PE difficult. To assess the diagnostic value and inter-observer agreement of magnetic resonance angiography (MRA) in a cohort of patients with suspected PE, we conducted a prospective clinical study. MRA was compared for sensitivity and specificity to a diagnostic strategy including clinical probability, D-dimer testing, spiral CT, ultrasound leg compression and pulmonary angiography. A total of 89 patients with clinically suspected PE were included: the clinical probability of PE was intermediate or high in 78, and low in the remaining 11. All patients underwent mono- or multi-slice spiral CT and MRA with gadolinium injection (both within 24 hours of entry to the study). Anticoagulation was withheld in patients concerned about the strategy. All subjects were followed up for 3 months. MRA was read independently by two experienced teams of radiologists: one local and one from another university centre. Spiral CT was positive in 62 of 63 cases of confirmed PE. No patient with negative CT findings was positive ultrasonographically. Only one patient with a negative CT (and negative ultrasound) had a recurrent thromboembolic event. The first team diagnosed PE with MRA in 47 cases, with a sensitivity of 71% and a specificity of 92%; the second team obtained the diagnosis in 23 cases, with a sensitivity of 31% and a specificity of 85%. Inter-observer agreement between MRA reading was low: Kappa = 0.16 (-0.01 to 0.33); p = 0.07. In conclusion, compared with an invasive strategy based on spiral CT, the diagnostic value of MRA is limited by poor inter-observer agreement.

Keywords
Venous thromboembolism, pulmonary embolism, magnetic resonance angiography

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Introduction
Pulmonary embolism (PE) is a common and potentially fatal disorder with an estimated annual incidence of 69 per 100,000 (1). Non-specific findings make the clinical diagnosis of PE difficult, and several studies have shown that its true prevalence among suspected cases is, at best, only 30% (2, 3).

Non-invasive approaches have proven accuracy and cost-effectiveness in the diagnosis of PE. In brief, they assess the likelihood of the condition on the basis of a combination of clinical findings, including plasma D-dimer concentrations, and the results of ventilation-perfusion lung scanning, and venous compression ultrasonography of the legs. Although pulmonary angiography remains the gold-standard diagnostic test, and is still considered necessary in 4% to 11% of cases of suspected PE (2, 3), the drawbacks are that it is invasive, it may produce results that are difficult to interpret, and is not readily available in many centres. Against that background, increasing interest has been expressed in the performance of contrast-enhanced spiral computed tomography (CT) of the chest in the diagnosis of acute PE (4–9). The specificity of CT in this context is very high, generally above 97%, and a thrombus found on spiral CT in a segmental or more proximal pulmonary artery is generally deemed to establish the diagnosis of PE.

The sensitivity of CT remains controversial, with reported figures ranging from 53% to 100% (10). However, technical re-
finements such as multi-row spiral CT have resulted in improved sensitivity, and recent evidence suggests that a combination of spiral CT and leg compression ultrasonography may be more sensitive than spiral CT alone (11–13). Nevertheless, because of the need to inject iodinated contrast media, spiral CT should be avoided in patients with renal insufficiency or a history of severe reaction to contrast media. As these conditions cannot always be detected or anticipated in emergency situations, there is a case for developing non-invasive diagnostic tools with no such limitations. Another issue is that chest examination requires a radiation dose of approximately 8 mSv, and even higher doses are needed when the pelvis or a lower limb is being investigated (14).

It has been suggested that magnetic resonance angiography (MRA) may be safer than CT as a result of the reduced risk of allergy to contrast agents, the lack of renal toxicity associated with low doses of contrast media, and freedom from ionising radiation. Preliminary studies suggest that the sensitivity and specificity of MRA in cases involving segmental or larger pulmonary embolisms are similar to those obtained with spiral CT (15–18).

The present prospective study is designed to assess the diagnostic value of MRA in a cohort of patients with suspected PE. MRA was interpreted in a blinded fashion, and the diagnostic standard for PE was established using a validated strategy (13–19) comprising a combination of clinical probability of PE, plasma D-dimer levels, and the results of spiral CT, compression ultrasonography of the legs, and pulmonary angiography. All patients were followed up for 3 months.

Methods

Patients

One hundred and fifteen patients with clinically suspected PE were recruited between October 1998 and June 2001. Patients were to meet the following inclusion criteria: they were in- or out-patients with a suspicion of PE, examined by one senior physician participating in the study; patients were evaluated for clinical probability of PE and included if probability was intermediate or high whatever D-dimers level as well as patients with low probability and D-dimers > 500ng/ml; patients who gave informed consent. Exclusion criteria were: age under 18 years, pregnancy, renal insufficiency (serum creatinine level more than 200 mM), documented allergy to contrast media, refusal or inability to consent to the study, massive PE with haemodynamic instability, clinically suspected deep venous thrombosis (DVT) at admission with no sign of pulmonary embolism, and contraindications to MRI such as the presence of a cardiac pacemaker, metal in the orbit, or an intracranial vascular clip. During the study period, 482 other patients with suspected PE underwent spiral-CT for diagnostic purposes but are not included here because the patient or physician declined or because the patient did not meet the inclusion criteria. Thus, only 19% of 597 patients with suspected PE were included.

Patients initially enrolled were excluded from further participation in the study if they received thrombolytic therapy between spiral CT and MRI examination, were lost to follow-up, or if their data were incomplete.

The protocol was approved by the Comité de Protection des Personnes pour la Recherche Biomédicale (Ethics Committee of Lorraine, France), and written informed consent was obtained from all participants. The study was funded by the French Ministry of Health (Programme Hospitalier de Recherche Clinique 1997).

Study design

The study was designed as a prospective management trial with a 3-month follow-up period. All patients underwent what was considered the gold standard diagnostic strategy, combining assessment of the clinical probability of PE, plasma D-dimer levels, and findings of spiral CT, compression ultrasonography of the legs and pulmonary angiography. MR angiography was performed after CT within 24 h of entry to the study and the results were later compared to those of the definitive diagnostic strategy. MRA findings were not taken into account when determining the patient’s management.

A pragmatic approach was adopted whereby the best CT-scan available was employed. Consequently, the same diagnostic algorithm was applied regardless which of the two machines was used. Since MRA was the technique under investigation, the same unit was used throughout. MRA findings were interpreted by two blinded, independent, experienced teams. Although the diagnostic criteria were clearly defined and recorded on standard topographic evaluation forms, in order to replicate real-life clinical conditions as closely as possible, readers were allowed no practice sessions on the sequences and images.

Patients were enrolled in the study by emergency room physicians responsible for their care, and underwent clinical assessment before any diagnostic testing in order to avoid bias. Plasma D-dimer ELISA testing was performed in all cases, and further diagnostic investigation depended on the pre-test clinical probability of PE.

Pre-test clinical probability of PE

The clinical probability of PE was assessed empirically by the physician in charge of the patient on the basis of risk factors for venous thromboembolism, symptoms and signs commonly encountered in PE, blood gases, chest radiographic findings, and the likelihood of another diagnosis. Clinical probability was rated as low, intermediate or high using criteria reported by Perrier et al. (2). Plasma D-dimer ELISA was conducted in all cases (D-dimer VIDAS BioMérieux France).

Diagnosis and management strategies (diagnostic algorithm)

In cases with a low probability of PE, a plasma D-dimer concentration <500 mg/l was deemed to rule out PE. Patients with a D-dimer concentration of 500 mg/l and above proceeded to spiral CT and MR angiography. If CT examination confirmed the diagnosis of PE, no other investigation was performed. If spiral CT was negative, the patient underwent compression ultrasonography of the legs. If the latter revealed a venous thrombosis, a diagnosis of PE was recorded and no further examination was performed. If no venous thrombosis was noted, pulmonary angiography was performed unless a documented alternative diagnosis could be obtained.
Patients in whom the probability of PE was intermediate or high underwent spiral-CT and MR angiography. If CT examination confirmed the diagnosis of PE, no more investigation took place. If spiral CT was negative, a plasma D-dimer concentration <500 mg/l was deemed to rule out PE. Patients with a D-dimer concentration of 500 mg/l and above proceeded to compression ultrasonography of the legs. If the latter revealed a venous thrombosis, a diagnosis of PE was recorded and no other examination was performed. If no venous thrombosis was noted, pulmonary angiography was performed unless a documented alternative diagnosis could be obtained.

In all cases, imaging was conducted within 48 h of entry to the study. Patients underwent diagnostic investigations on anticoagulation with unfractionated heparin or tinzaparin. When the diagnosis of PE was excluded, anticoagulation was withheld.

MR angiography was analysed independently of the algorithm and not taken into account in the subsequent management strategy.

Follow-up
All patients were seen or interviewed by phone by one of the study investigators at 6 weeks and 3 months. The family physician was contacted whenever the interim history revealed a possible event. Critical events recorded by the investigators during follow-up were: death, bleeding complications, and venous thromboembolic events (deep venous thrombosis [DVT] and PE). All critical events were assessed by an adjudication committee. Patients were judged to have PE during follow-up when a new thrombus was identified with spiral-CT. Deep-vein thrombosis during follow-up was confirmed when a new thrombus was found with ultrasonography. The adjudication committee also classified deaths during follow-up (on the basis of all available information) as: definitely related to PE, possibly related to PE (if the cause of death could not be clearly established), or definitely not related to PE. Finally, the committee reviewed the safety data at regular intervals throughout the study. Recruitment of patients was discontinued if the rate of venous thromboembolic events was higher than expected (i.e. above 3%) in patients from whom treatment was withheld. All adverse events were reported to the funding source.

Diagnostic techniques
Spiral CT
A single-detector-row spiral CT (Somatom Plus 4A with ultra fast ceramic detectors, Siemens, Erlangen, Germany) was used until August 16th 1999, after which it was replaced by a multi-detector-row CT with four detector arrays (Somatom VZ, Siemens). For single-detector-row spiral CT, collimation of 2.0 mm was used with a pitch of 1.8 to 2.2 and 0.75 second gantry rotation. Multi-detector-row multi-slice CT used a collimation of 1 mm (4 x 1 mm) with a pitch of 1.5 to 2 and a 0.5 sec gantry rotation. A power injector (Medrad) was used to administer a total of 120 to 150 ml of Iobitiridol with an iodine concentration of 300 mg I/ml (Xenetix® 300, Guerbet, Villepinte, France) with an injected rate of 3 to 4 ml/sec. A bolus chasing system (Carebolus®, Siemens) was used whenever possible to achieve high and uniform contrast enhancement throughout the thorax.

MR-angiography
All pulmonary MR angiograms were obtained by using a 1.5T Signa EchoSpeed (General Electric Medical Systems, Milwaukie, USA) and a standard torso-array coil. 3D-Gadolinium-enhanced MRA was conducted using a 3D spoiled gradient-echo sequence in the coronal, axial and sagittal planes in all patients with the following parameters: TR/TE/a= 4.9 to 6.7 ms/1.4 ms /25°. The bandwidth was 62.5 kHz. The field of view was 48 x 36 cm for coronal acquisitions and 48 x 24 cm for axial and sagittal acquisitions. Slice thickness was 3.4 to 4.2 mm. The acquisition time, number of slices, matrix size and number of excitations were determined by the ability of the patient to hold his or her breath. Acquisition time ranged between 7 and 34 seconds, the number of slices ranged between 12 and 40 and the number of excitations was 1 or 0.5. Matrix size was 256 x 160–192.

Patients were asked to hyperventilate for 30 sec before acquisition, which was obtained in deep inspiration. A total of 40 ml of gadodiamide (Omniscan®, Amersham Health) was injected using a power injector (MR Spectris; Medrad).

Acquisitions were obtained in the three planes because these images are usually of much better quality than multiplanar reformations (MPR) which are altered by anisotropic voxels. In the coronal plane, two acquisitions were performed 15 sec apart, with an injection of 20 ml of gadodiamide at a rate of 1.5 ml/sec followed by a 20 ml saline chaser. Correct timing of the injection was accomplished using a gadolinium detection pulse sequence (SmartPrep®, General Electric Medical Systems). One acquisition was then obtained in the axial plane with injection of 20 ml of gadodiamide at a rate of 1.5 ml/sec followed by a 20 ml saline chaser. Finally, a sagittal acquisition was performed with no additional injection.

Ultrasonography
Bilateral venous compression ultrasonography of the legs was performed from the common femoral vein to the trifurcation of the calf veins, inclusive. Lack of vein compressibility was taken as diagnostic of deep-vein thrombosis. In the other cases, ultrasonography was judged negative.

Pulmonary angiography
Pulmonary angiography was performed and interpreted by a senior radiologist who did not interpret the MRA (to avoid bias) but who did have access to the patient's case notes and spiral CT findings. Selective catheterisation of the right and left pulmonary arteries was undertaken. All patients underwent two acquisitions per lung (with the selective technique). Additional sub-selective injections were given when the findings of the selective injections were non-diagnostic. PE was diagnosed if an intra luminal filling defect or a sharp cut-off in a vessel of at least 2 mm in diameter was detected.

Image interpretation
Spiral CT
Images were interpreted by consensus between a junior and a senior radiologist on films with mediastinal and lung window settings and on a workstation with cine mode and multiplanar reformations (MPR). Radiologists were aware of the clinical probability of PE but not of the D-dimer concentration, other
than in patients with a low probability of PE, whose D-dimer concentration was above 500 mg/l, according to the protocol. PE was diagnosed if a central filling defect outlined by contrast material or complete occlusion was seen in a sub-segmental or more proximal pulmonary artery (Figs. 1, 2). Spiral CT was judged negative for the diagnosis of PE when pulmonary arteries, including all segmental branches, were visualised and determined to be free of thrombus, and no thrombus was detected in a sub-segmental pulmonary artery. Interpretation was reported on standardized forms.

**MR-angiography**
Images were interpreted independently by two teams of radiologists. A first interpretation was obtained by consensus between a junior and a senior local radiologist (not those who interpreted the spiral CT findings) immediately after MRA examination to simulate an emergency. Radiologists were blinded to the results of spiral CT and, as in spiral CT interpretation, they were aware of the clinical probability of PE but not of the D-dimer concentration, other than in patients with a low probability of PE whose D-dimer concentration was by definition above/L. Images were analysed on film and using a computer workstation (Advantage Windows 3.1; GE Medical Systems) with cine mode, MPR and multi-projection volume reconstructions (MPVR).

A second interpretation was obtained by consensus between two experienced radiologists (PD, AM) from an independent university hospital. All MR examinations were recorded on CD-ROM and sent to the radiologists, who were blinded to the results of the diagnostic strategy. Image analysis was conducted on a Theralyys workstation (Creatis, Lyon, France) using cine mode and MPR.

PE was diagnosed if a central filling defect outlined by contrast material or complete occlusion was seen in a sub-segmental or more proximal pulmonary artery (Figs. 1, 2). All sequences relating to a particular patient were analysed in one session, in order to optimize vessel identification and avoid false positive diagnoses due to flow-related artefacts (although the

**Figure 1: Multi-row spiral CT and MRA in an 83-year-old female patient with massive acute pulmonary embolism.** The time for each MRA acquisition was 14 sec. A-C. Spiral-CT shows multiple emboli (arrows). D-G. First pass MRA coronal acquisition (D, E) and second coronal acquisition (F, G) demonstrate thrombi in the main arteries (straight arrows) and in the left segmental medio-basal artery (curved arrow). Note that the right lower lobe arteries are not visible suggesting a proximal thrombus. H-I. Axial acquisition performed at the same level as A and B, highlighting the floating thrombus (black arrow). Obstructed arteries are hardly visible (arrow head). Both team of radiologists agreed on the diagnosis of PE.
latter are reduced by the use of contrast-enhanced MRA). MRA was judged negative for the diagnosis of PE when pulmonary arteries, including all segmental branches, were visualized and seen to be free of thrombus and no thrombus was detected in a subsegmental pulmonary artery. Interpretation was reported on standardized forms.

Ultrasonography
Lack of vein compressibility was taken as diagnostic of deep-vein thrombosis. In the other cases, ultrasonography was judged negative.

Pulmonary angiography
PE was diagnosed if an intraluminal filling defect or a sharp cut-off in a vessel of at least 2 mm in diameter was seen.

Statistical analysis
Demographic and clinical data related to non-included and included patients were analysed using Student’s t test for quantitative variables and c² for categorical data. Included patients were also compared to those with an intermediate or high probability of PE and those with a low probability of PE.

Sensitivity, specificity, and positive and negative predictive values for the detection of PE with MR angiography were calculated for both teams of radiologists. The Cohen kappa test was used to determine the degree of agreement between MR angiography and spiral CT, and between the MRA readings of the two different teams of radiologists for the diagnosis of PE. Finally, the degree of agreement between MR angiography and spiral CT was determined for each pulmonary artery. All results included 95% confidence intervals.

Results
Of the 115 patients recruited, 26 were excluded during the study for one or more of the following reasons: withdrawn consent (n=5), difficulties with follow-up (n=3), MRI examination not performed (n=10), incomplete data (n=4), angiography not per-
formed (n=7), diagnostic strategy inconsistent with the protocol (n=3). Although 13 patients had poor or moderate image quality on MRA, none were excluded (in order to avoid selection bias).

The median age of the remaining 89 patients was 68.8 years. Table 1 compares included patients to the non-included group. Seventy-eight patients included in the prospective study presented with an intermediate or high probability of PE, and in 11 the probability was low. A single-detector-row spiral CT was used in 36 cases, and a multi-detector-row CT in 53.

No statistically significant differences in demographic or clinical data were observed between the two groups of patients, other than in varicose status (Table 2).

Among 78 patients with an intermediate or high probability of PE, diagnostic workout is reported in figure 3. PA was not performed in three cases because the patients were frail, and in two cases another diagnosis was made using spiral-CT. In the latter, anticoagulation was withheld and no further DVT or PE was diagnosed during follow-up. However, PE was diagnosed in one patient who underwent repeat spiral CT 6 weeks later because of recurrent symptoms. A false-negative finding was recorded.

In patients with low probability of PE who exhibited D-dimer plasma levels of 500 mg/l and above diagnostic workout is reported in figure 4. Three patients were too frail for PA. However, in all cases, an alternative diagnosis was obtained with spiral-CT and anticoagulation was withheld and no further VTE was diagnosed during follow-up. Overall, the diagnosis of PE was retained in 63 cases.

Readings of MRA by the two independent teams of experienced radiologists yielded the following results. Local radiologists made a diagnosis of PE in 47 cases, with a sensitivity of 71% (95% CI: 60–82), a specificity of 92% (82–100), a positive predictive value of 96% (90–100), and a negative predictive value of 57% (42–72). The other team made the diagnosis in 23 cases, with a sensitivity of 31% (19–42), a specificity of 85% (71–98), a positive predictive value of 83% (67–98) and a negative predictive value of 34% (20–47) (Table 3).

The kappa agreement test between the MR reading of the two different teams of radiologists was low (kappa=0.16 [-0.01–0.33]; p=0.07). The kappa agreement test between MR

Table 1: Characteristics of included and non-included patients referred for suspected PE during the study period.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Included patients (n=89)</th>
<th>Non included patients (n=482)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean, SD) yr</td>
<td>64 (±16)</td>
<td>66.9 (±19)</td>
<td>0.13</td>
</tr>
<tr>
<td>Female (%)</td>
<td>49.4%</td>
<td>59%</td>
<td>0.06</td>
</tr>
<tr>
<td>Positive CT</td>
<td>69.7%</td>
<td>32.4%</td>
<td>&lt;10⁻⁴</td>
</tr>
<tr>
<td>Cancer</td>
<td>7%</td>
<td>10%</td>
<td>0.34</td>
</tr>
</tbody>
</table>

Table 2: Characteristics of the two groups of included patients.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Included patients with low probability of PE (n=11)</th>
<th>Included patients with intermediate or high probability of PE (n=78)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean, SD) yr</td>
<td>63 (±18)</td>
<td>64 (±15)</td>
<td>0.85</td>
</tr>
<tr>
<td>Female (%)</td>
<td>36%</td>
<td>51%</td>
<td>0.52</td>
</tr>
<tr>
<td>History of VTE</td>
<td>0%</td>
<td>24%</td>
<td>0.11</td>
</tr>
<tr>
<td>Family history of VTE</td>
<td>0%</td>
<td>20.5%</td>
<td>0.20</td>
</tr>
<tr>
<td>Varicose status</td>
<td>0%</td>
<td>51%</td>
<td>&lt;10⁻²</td>
</tr>
<tr>
<td>Vena cava filter</td>
<td>0%</td>
<td>2.9%</td>
<td>1.00</td>
</tr>
<tr>
<td>Obesity</td>
<td>20%</td>
<td>33.8%</td>
<td>0.48</td>
</tr>
<tr>
<td>Cardiac disease</td>
<td>30%</td>
<td>28%</td>
<td>1.00</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease</td>
<td>11.1%</td>
<td>8.1%</td>
<td>0.57</td>
</tr>
<tr>
<td>History of stroke</td>
<td>11.1%</td>
<td>2.7%</td>
<td>0.29</td>
</tr>
<tr>
<td>Cancer</td>
<td>0%</td>
<td>8%</td>
<td>1.00</td>
</tr>
<tr>
<td>Recent surgery</td>
<td>11.1%</td>
<td>13.3%</td>
<td>1.00</td>
</tr>
<tr>
<td>Recent trauma</td>
<td>11.1%</td>
<td>10.7%</td>
<td>1.00</td>
</tr>
<tr>
<td>Recent bed rest</td>
<td>0%</td>
<td>16.2%</td>
<td>0.34</td>
</tr>
<tr>
<td>Oral-contraceptive use</td>
<td>0%</td>
<td>5.4%</td>
<td>1.00</td>
</tr>
<tr>
<td>Hormone-replacement therapy</td>
<td>0%</td>
<td>10%</td>
<td>0.58</td>
</tr>
<tr>
<td>Post-partum</td>
<td>0%</td>
<td>0%</td>
<td></td>
</tr>
</tbody>
</table>

Figure 3: Results in the group of patients with intermediate or high probability of PE.
angiography read by the local team and spiral CT was moderate (kappa=0.56 [0.40–0.73]; p=10^{-4}) and the kappa agreement test between MR angiography read by the other team and spiral CT was poor (kappa=0.12 [-0.01–0.25]; p=0.11). The degree of agreement for detection of thrombi in each pulmonary artery ranged from –0.04 to 0.75.

**Discussion**

In this study, the accuracy of MRA in diagnosing PE was not sufficient to justify its use as part of a routine non-invasive strategy.

The first step of the present study was to determine whether a combination of examinations including spiral CT would be sufficiently sensitive and specific to reduce the need for pulmonary angiography in most cases. A particular diagnostic strategy was adopted according to the pre-test probability of PE. Its specificity relied on that of spiral CT, which several investigators have reported to be very high, potentially obviating the need for pulmonary angiography in most cases (7, 12, 13). Some recent studies strongly suggest that the sensitivity of spiral CT is high (7, 12). However, such findings remain controversial (Musset et al. reported that 9% of patients with negative spiral CT results were positive when assessed using ultrasound of lower limbs) (13). Therefore, we performed additional imaging techniques, including pulmonary angiography, when spiral CT was negative.

The rate of venous thromboembolic events was low (1.1%) over 3 months of follow-up in patients with suspected PE who were not given anticoagulant therapy on the basis of negative findings according to the strategy used here. More specifically, in the group of patients with low clinical probability of PE with negative spiral CT and ultrasonography, we did not diagnose pulmonary embolism in any patient by pulmonary angiography or 3 months follow-up. Thus, on the basis of these results as well as other studies, we can recommend that PA should not be performed in these low-probability patients (2, 13).

There is an undoubtedly significant selection bias in the present data. Only 19% of the total number of patients with suspected PE who underwent spiral CT during the study period are represented, and those included had a high prevalence of PE compared with the remainder. Only a small number of the patients included had a low probability of PE because of the decision to exclude those with a low clinical probability and negative D-dimer findings. The lack of differences in demographic or clinical data between patients with low and intermediate or high probability of PE (other than in varicose status), and the high frequency of PE in each group of patients suggest that the empirical probability of PE was underestimated. These selection biases can be explained by the reluctance of responsible physicians to schedule patients for possible PA, which is invasive. According to the algorithm, a high proportion of patients with a low probability of PE would have undergone PA.

**Table 3: Diagnostic performance of contrast-enhanced MR angiography.** Present results and those of previous studies. Values are given with 95% confidence intervals in brackets.

<table>
<thead>
<tr>
<th>Study</th>
<th>Number of patients</th>
<th>Gold standard</th>
<th>Frequency of PE</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Interobserver agreement for all vessels</th>
<th>Interobserver agreement for proximal vessels</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loubeyre, 1994</td>
<td>23</td>
<td>PA</td>
<td>52%</td>
<td>70%</td>
<td>100%</td>
<td>Not assessed</td>
<td>Not assessed</td>
</tr>
<tr>
<td>Meaney, 1997</td>
<td>30</td>
<td>PA</td>
<td>27%</td>
<td>100%</td>
<td>95%</td>
<td>0.57 [0.37–0.77]</td>
<td>0.83 [0.69–0.98]</td>
</tr>
<tr>
<td>Gupta, 1999</td>
<td>36</td>
<td>PA</td>
<td>36%</td>
<td>85% [64–98]</td>
<td>96% [85–100]</td>
<td>0.54 [0.27–0.81]</td>
<td></td>
</tr>
<tr>
<td>Oudkerk, 2002</td>
<td>118</td>
<td>PA</td>
<td>30%</td>
<td>77% [61–90]</td>
<td>98% [92–100]</td>
<td>0.75</td>
<td></td>
</tr>
<tr>
<td>Present study</td>
<td>89</td>
<td>algorithm</td>
<td>71%</td>
<td>71% [60–82]</td>
<td>92% [82–100]</td>
<td>0.16 [-0.01–0.33]</td>
<td>0.22 [0.06–0.39]</td>
</tr>
</tbody>
</table>

† Local team; ‡ Other team
The D-dimer assay used here was a rapid ELISA suited to emergency administration and with demonstrated high performance at a threshold of 500 μg/L (2). The D-dimer level was under 500 μg/L in only six of the present patients, ruling out the diagnosis of PE. The contribution of the D-dimer assay was lower than expected due to the small number of patients with a low pre-test probability of PE, and the high prevalence of proven PE.

Although these selection biases did not interfere with the final diagnosis, the inclusion of patients with a lower pre-test probability of PE may have influenced the findings regarding the performance of MRA. Given the high false negative rate and the lower false positive rate with MRA, a lower prevalence of PE would have biased the data in support of its diagnostic value.

The results of MRA reported here differ from those obtained in previous studies. In the first report on contrast-enhanced MRA, the sensitivity was 100% for proximal emboli but 0% for distal thrombi (15). In the three other published studies (16–18), the sensitivity was higher than here (Table 3). This may be explained by the diagnostic criteria established for MRA. In the present study, PE was recorded only when defects were identified in the same vessel on all sequences, while in other series only one sequence was analysed. The specificity of MRA is high and comparable across the different studies, but interobserver agreement varies markedly between investigations, and even within the same study. Interestingly, one paper reports higher interobserver agreement for segmental vessels than for main and lobar vessels (16). Several factors may play a role in the surprisingly low agreement between the two teams of radiologists reported here. First, the independent readers were blinded to data concerning the clinical probability of PE; second, despite being experienced radiologists, the readers may have been unfamiliar with the MRA images they were given; third, the local team analysed images on film and at a computer workstation, whereas films were not available for the second team. Finally, although interpretation was standardized, the multiple acquisitions may, paradoxically, have made the analysis of each specific vessel more difficult. In contrast to CT-scanning, which depicts all free and occluded vessels, MRA does not visualise thrombosed vessels, making the depiction of thrombi and the identification of each specific vessel more difficult. All these points underline the difficulty of interpreting MRA optimally when the examination is performed on an unfamiliar apparatus. The present findings suggest that the practical value of MRA in the diagnosis of PE can be improved by giving readers practice sessions with the machine concerned.

Discrepancies between studies may also be due to the types and numbers of patients included, the MR apparatus used and the type of sequence, the amount of injected contrast media, the diagnostic gold standard, the prevalence and characteristics of PE in the study group and finally, the number of patients excluded because of poor image quality (18, 20–25). The present authors’ decision to include the latter group in order to better reflect everyday clinical practice may lead to a lower assessment of diagnostic performance than is reported elsewhere. For example, Ouderkink et al. excluded 6% of patients for that reason (18).

In summary, the present study illustrates the weaknesses and limitations of MRA in the diagnosis of PE. Good specificity is associated with moderate sensitivity. As noted by Yucel (25), this technique should be considered only in patients with contraindications to iodinated contrast agents, and cannot be recommended as a standard feature of diagnostic algorithms. Shorter sequences with improved spatial resolution should be investigated for their value in diagnosing PE. The improvement of MR angiography techniques may improve its accuracy (26–28).

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Appendix

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