Gadolinium-Enhanced Magnetic Resonance Angiography for Detection of Acute Pulmonary Embolism

An In-depth Review

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Study objective: To review the published experience with gadolinium-enhanced magnetic resonance angiography (MRA) for the detection of acute pulmonary embolism (PE) in order to test the hypothesis that gadolinium-enhanced MRA may be potentially sensitive and specific enough to include it among diagnostic alternatives in the evaluation of patients with suspected PE.

Methods: Studies were identified by searching MEDLINE for trials that used gadolinium-enhanced MRA to diagnose acute PE based on the visualization of an intraluminal filling defect or a cutoff vessel, using pulmonary angiography as a reference standard.

Results: Twenty-eight investigations were identified in which MRA was used to diagnose PE. Only three studies, however, met the criteria for inclusion in the analysis. In these three case series, the sensitivity of gadolinium-enhanced MRA ranged from 77 to 100%, and the specificity ranged from 95 to 98%.

Conclusion: Gadolinium-enhanced MRA may be a useful diagnostic alternative in some patients with suspected acute PE, particularly if they have an elevated creatinine level, have an allergy to radiographic contrast material, or should, if possible, avoid exposure to ionizing radiation.

Key words: gadolinium; magnetic resonance angiography; pulmonary embolism; pulmonary thromboembolism

Abbreviations: CI = confidence interval; MRA = magnetic resonance angiography; PE = pulmonary embolism

Diagnostic strategies for acute pulmonary embolism (PE) have evolved over the last several decades with the development of new diagnostic methods. These started with pulmonary angiography about 4 decades ago, and were followed by ventilation-perfusion lung scintigraphy, objective leg tests for a surrogate diagnosis of PE, d-dimer assay for the exclusion of PE, digital subtraction pulmonary angiography, contrast-enhanced spiral CT scanning, and, most recently, magnetic resonance angiography (MRA).1 Many of these diagnostic tests continue to be evaluated and refined, and their roles, alone or in combination, continue to evolve. Contrast-enhanced spiral CT scanning has a particularly wide appeal and has been adopted at many centers, although the procedure is still undergoing extensive evaluation in a national collaborative investigation, the Prospective Investigation of Pulmonary Embolism Diagnosis II.2

The purpose of this review, therefore, was to evaluate the published experience with gadolinium-enhanced MRA for the detection of acute PE to test the hypothesis that it may be potentially sensitive and specific enough to include it among diagnostic alternatives in the evaluation of patients with suspected PE. Patients who are allergic to contrast material, who have a high serum creatinine level, or who should avoid ionizing radiation, if possible, would be likely to benefit from MRA. However, pregnant patients can be evaluated for PE using standard techniques such as ventilation-perfusion lung scans and pulmonary angiography via the me-
MRA, for the MRA data had not been acquired three-
were as follows: an objective diagnostic test had not
for more than one reason. The reasons for exclusion
investigations failed to meet the criteria for inclusion
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enhanced MRA only for perfusion imaging, studies
had researched chronic thromboembolic hypertension
rather than acute PE, or studies had not used gadolinium-enhanced MRA.

Three investigations met the criteria for inclusion in the analysis. The diagnostic reference standard for PE in each of these investigations was pulmonary angiography. Patients in the study were consecutive patients with suspected acute PE who had been referred for pulmonary angiography. Patients were excluded if there was a contraindication to MRA. In one investigation, patients were excluded if they were receiving mechanical ventilation. Imaging techniques used in these investigations are shown in Table 1. The results of the individual investigations are shown in Table 2. In these three case series for the diagnosis or exclusion of PE, the sensitivity of gadolinium-enhanced MRA ranged from 77 to 100%, and the specificity ranged from 95 to 98% (Table 2).

**RESULTS**

We identified 28 investigations in which MRA was used to diagnose PE. Many of these, however, did not meet the criteria for inclusion in our study. Some investigations failed to meet the criteria for inclusion for more than one reason. The reasons for exclusion were as follows: an objective diagnostic test had not been ordered independently of the results of the MRA, the MRA data had not been acquired threedimensionally (and may not have used gadolinium), or some of the patients were not suspected of having PE or had had not undergone a definitive diagnostic test. Tests were observational and did not test sensitivity and specificity, tests used gadolinium-enhanced MRA only for perfusion imaging, studies had researched chronic thromboembolic hypertension rather than acute PE, or studies had not used gadolinium-enhanced MRA.

**Materials and Methods**

**Study Identification**

We attempted to identify all published trials that used gadolinium-enhanced MRA to diagnose acute PE. Two independent MEDLINE searches were obtained from 1987 to 2002 using the key words pulmonary embolism and magnetic resonance imaging. We augmented our searches by manually reviewing the reference lists of all original articles and all review articles. This was done by two of the authors working together (PDS and FK).

**Study Eligibility**

Each study was evaluated for inclusion by two investigators. Any disagreements were resolved by discussion. Investigators were not blinded to journal, author, or institution. Studies were included if they met all of the following criteria: (1) the diagnosis of PE had been made on the basis of objective tests; (2) patients had been studied consecutively; (3) the study had been performed prospectively; (4) all MRA images were obtained with gadolinium as a contrast agent; (5) the criteria for the diagnosis of PE by MRA was visualization of an intraluminal filling defect or a cutoff vessel; (6) the data acquisition was three-dimensional; (7) gadolinium-enhanced MRA and the diagnostic tests for PE were interpreted independently; (8) all patients studied were suspected of having PE; (9) the study included patients with and without PE; (10) the decision to perform the reference diagnostic test was made independently of the MRA result; (11) descriptions of the MRA methods were sufficiently detailed to permit replication; and (12) sensitivity and specificity, or the raw data for these calculations, were presented.

**Data Synthesis and Statistical Analysis**

Sensitivity was calculated as the percentage of patients with PE in whom MRA showed the presence of a PE. Specificity was calculated as the percentage of patients who did not have a PE and in whom MRA did not show a PE. The 95% confidence interval (CI) was determined from the normal approximation to the binomial distribution.

**DISCUSSION**

The strength of the data on the use of gadolinium-enhanced MRA for the diagnosis of acute PE is limited because the data are sparse. There were more data on the specificity of gadolinium-enhanced MRA than on its sensitivity. The evaluation of the sensitivities of individual investigations requires caution because of the small sample sizes. Pooling may give an impression based on more patients, but patient demographics were not stated and there were differences in MRA technique. The overall estimate of the sensitivity and specificity derived from pooling, therefore, may serve as a preliminary guide, but further studies are needed.

While overall the imaging techniques used in the three included investigations of gadolinium-enhanced MRA were similar, there are a few notable differences. First, Meaney et al. used a triple dose of contrast agent, compared with the dose of IV gadolinium used by Oudkerk et al. and Gupta et al. Of note, in the article by Meaney and col-

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**Table 1—Imaging Techniques Used for Gadolinium-Enhanced MRA for Diagnosing Acute PE**

<table>
<thead>
<tr>
<th>Matrix</th>
<th>Field of View, cm</th>
<th>Section Thickness, mm</th>
<th>Study</th>
</tr>
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<tbody>
<tr>
<td>(90–106) × 512</td>
<td>20 × 32</td>
<td>1.25†</td>
<td>Oudkerk et al.</td>
</tr>
<tr>
<td>140 × 256</td>
<td>31 × 35</td>
<td>3.4</td>
<td>Gupta et al.</td>
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</tbody>
</table>

*All studies used a 1.5-Tesla system.
†Reconstructed from 2.8 mm.
leagues, while the consensus sensitivity was 100%, the average sensitivity of the three blinded readers prior to the consensus reading was 87%, which is more in keeping with the results of the other studies.

A second difference is that while Oudkerk and colleagues used a technique with a relatively high spatial resolution, they imaged each lung sagittally and then constructed coronal and axial images from this data set, using all three planes for interpretation. Constructed images in the axial and coronal planes have poorer resolution than the original images obtained in the sagittal plane. In the other studies, images were acquired and read in the coronal plane, although Meaney and colleagues permitted the creation of additional images in operator-defined planes. These differences in data acquisition and image interpretation may or may not have contributed to the lower sensitivity reported by Oudkerk and colleagues.

The preliminary experience using MRA for acute PE without a contrast agent, in small case series, showed either a high sensitivity, but suboptimal specificity, or vice versa. A variety of imaging techniques were used. Grist and colleagues, among 12 patients with PE, showed a sensitivity of 92 to 100%, but among 8 patients in whom PE was excluded, specificity was only 62%. Erdman and colleagues, among 21 patients with PE, showed a sensitivity of 90%, but among 13 patients in whom PE was excluded, specificity was 77%. Moody and colleagues, in four patients showed a sensitivity of 100%, but the specificity in nine patients was 67%. On the other hand, among 53 patients, expert readers of MRA showed a sensitivity of 71% and a specificity of 97%.

The use of MRA of the pulmonary vasculature has been hampered by artifacts due to respiratory and cardiac motion, poor signal-to-noise ratio, long image acquisition times, and limited spatial resolution. These drawbacks have been overcome by improvements in hardware and software and by the use of magnetic resonance contrast agents. Contrast-enhanced MRA is more robust than MRA techniques that do not use a contrast agent. The added signal provided from the contrast agent permits increased spatial resolution and reduces artifacts within the blood pool, thereby increasing vascular signal homogeneity. Current techniques permit high-resolution (512 matrix) imaging during a single breath-hold of 20 to 25 s or thinner slices (1.0 to 1.25 mm). Patients with a decreased capacity to hold their breath can undergo moderate-resolution imaging (256 matrix) during a shorter breath-hold.

Some investigators have used gadolinium-enhanced MRA to show pulmonary perfusion based on the filling of small vessels. This is analogous to the perfusion phase of a pulmonary angiogram, which has been shown to be useful but nonspecific. It is also analogous to a perfusion lung scan. The most appealing approach to the application of gadolinium-enhanced MRA is its potential use for showing intraluminal filling defects. The intraluminal filling defect was shown to be a diagnostic feature on pulmonary angiograms, and it continues to be considered the characteristic that is diagnostic of PE.

Gadolinium-enhanced MRA potentially can be used to image the veins of the pelvis and lower extremities as well as the pulmonary arteries during the same examination. Experience with MRA, even without the use of a magnetic resonance contrast agent, for the detection of proximal deep venous thrombosis and extension into the pelvic veins has shown a sensitivity of 94 to 100% and a specificity of 90 to 100%. Contrast-enhanced MRA following injection of the contrast medium into a pedal vein, showed postthrombotic changes with a sensitivity of 100% (13 of 13 patients) and a specificity of 98% (58 of 90 patients).

Our article reviewed clinical trials that implemented the latest MRA technology (breath-hold contrast-enhanced, volumetric [three-dimensional], gradient-recalled echo techniques). Yet, since these articles were written, MRA technology has continued to improve. Intravascular contrast agents, which remain in the blood pool longer than conventional gadolinium-based contrast agents, are currently in phase III US Food and Drug Administration trials and may soon be on the market. Because of their long intravascular half-life, these agents maintain a higher concentration within the blood pool than conventional agents, and have the potential of providing both a better signal and improved blood pool contrast against the low-signal-intensity pulmonary embolus. In addition, the deep venous system of the lower extremity potentially can be evaluated in the same examination without the administration of an additional contrast agent.

Table 2—Gadolinium-Enhanced Pulmonary MRA for Acute Pulmonary Embolism

<table>
<thead>
<tr>
<th>Study</th>
<th>Sensitivity*</th>
<th>Specificity†</th>
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<tbody>
<tr>
<td>Meaney et al</td>
<td>8/8 (100)</td>
<td>21/22 (95)</td>
</tr>
<tr>
<td>Oudkerk et al</td>
<td>27/35 (77)</td>
<td>81/83 (98)</td>
</tr>
<tr>
<td>Gupta et al</td>
<td>11/13 (85)</td>
<td>22/23 (96)</td>
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</tbody>
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*Values given as No. of patients showing PE on MRA/total No. of patients with PE (%).
†Values given as No. of patients showing no PE on MRA/total No. of patients with no PE (%).
Based on a sample of 7,889 patients with suspected PE who were evaluated for recruitment into the Prospective Investigation of Pulmonary Embolism Diagnosis II, 3% were pregnant, 4% were allergic to iodinated contrast material, and 19% had an elevated serum creatinine level. One or more were present in 24%. The data are insufficient to recommend where gadolinium-enhanced MRA might fit in a diagnostic pathway for PE. With the present state of the art and its limited availability, it is likely that gadolinium-enhanced MRA would be most useful in patients with a strong suspicion of PE, in whom the results of other tests are equivocal and radiographic contrast material or ionizing radiation are relatively contraindicated.

REFERENCES
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