Diagnosis of Pulmonary Arterial Hypertension and Pulmonary Embolism With Magnetic Resonance Angiography*

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Background: Pulmonary magnetic resonance angiography (PMRA) has been proven to be accurate for the diagnosis of suspected acute or chronic pulmonary embolism (PE). Only limited data exist on the reliability of PMRA for the diagnosis of acute and chronic pulmonary artery hypertension (PAH). The aim of this study was to determine the accuracy of PMRA in the differentiation between patients suffering from PAH of varying etiologies.

Methods: Fifty patients (21 women; mean [± SD] age, 52 ± 16 years) were examined with gadolinium-enhanced PMRA for the evaluation of pulmonary artery (PA) disease. The diagnosis of PAH (ie, systolic PA pressure of > 35 mm Hg) was determined by Doppler echocardiography. The criteria for the diagnosis of chronic PAH by PMRA were dilated central PAs (diameter > 28 mm) and abnormal proximal-to-distal tapering of the PAs. The diagnostic criterion for acute and chronic PE was the presence of an intravascular filling defect.

Results: Chronic PAH was present in 18 patients, which was correctly identified by PMRA in 16 patients (sensitivity, 89%). All patients without PAH had normal findings on PMRA (specificity, 100%). Only 1 of 18 patients with normal findings on PMRA showed moderate chronic PAH (negative predictive value, 94%). PAH due to acute/subacute pulmonary thromboembolism (15 patients) was identified in all patients (sensitivity, 100%). Acute PAH was differentiated from chronic PAH in all cases by the detection of intravascular filling defects and the lack of abnormal proximal-to-distal tapering of PAs.

Conclusions: PMRA is a promising noninvasive imaging modality for the identification of patients with acute or chronic PAH. This technique should be considered a sensitive and highly specific screening tool for suspected chronic PAH.

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Key words: magnetic resonance angiography; pulmonary embolism; pulmonary hypertension

Abbreviations: Dp = peak pressure difference between right ventricle and atrium; PA = pulmonary artery; PAH = pulmonary artery hypertension; PE = pulmonary embolism; PMRA = pulmonary magnetic resonance angiography; RPAD = right pulmonary artery diameter; TR = tricuspid regurgitation

Pulmonary arterial hypertension (PAH) is a common problem in patients with heart failure, COPD, or interstitial pulmonary disease as well as acute and chronic pulmonary embolism (PE). The development of PAH is an important contributor to exercise intolerance. The severity of PAH correlates to the extent of dyspnea and the prognosis of these patients. However, treatment of the various underlying diseases is very different. An accurate diagnosis of the etiology is therefore essential.

Imaging studies can contribute to the care of patients with PAH. They help to detect its presence, indicate possible causes, quantify its severity, and allow the evaluation of the functional state of the right ventricle.

An echocardiographic Doppler examination can provide a noninvasive estimation of the pulmonary artery (PA) pressure, but it often does not allow a clear etiologic determination of PAH.

Pulmonary magnetic resonance angiography (PMRA) is a new promising noninvasive imaging technique, which has been reported to have a high sensitivity and specificity in the diagnosis of PE without the need for ionizing radiation or iodinated...
contrast material. The usefulness of PMRA in the diagnostic workup of other diseases involving the PA circulation has not been extensively studied.

The aim of this study was to determine the accuracy of PMRA in distinguishing patients with various etiologies of PAH.

Materials and Methods

Patients

The study population consisted of 50 consecutive patients (21 women; mean [± SD] age, 52 ± 16 years) who underwent PMRA for the evaluation of suspected pulmonary or PA disease. Patients with contraindications for an MRI study, patients requiring mechanical ventilation, patients with a missing signal of tricuspid regurgitation (TR) in the echocardiographic Doppler study, and patients who declined to participate in the study were excluded from the study. Informed consent was obtained from all patients. Each patient underwent a clinical evaluation, PMRA, and echocardiographic Doppler examination.

Echocardiographic Doppler Studies

All echocardiographic Doppler studies were performed with the patient in the resting state within 24 h before the PMRA was performed. M-mode, two-dimensional, and Doppler echocardiography were performed from the standard parasternal, apical, and subcostal views with the patient in the supine or left lateral positions. PA systolic pressure was calculated by adding the right atrial pressure, which was assumed to be 5 mm Hg in all cases, to the peak pressure difference between right ventricle and atrium (Dp). Dp was calculated from the continuous-wave Doppler signal of the TR gradient by the use of the simplified Bernoulli equation (Dp = 4v², where v is the peak flow velocity of the tricuspid regurgitant jet). The velocities in the tricuspid regurgitant jet were obtained from the apical four-chamber view. PAH was defined as a calculated PA systolic pressure of > 35 mm Hg.

MRI

All patients were studied with a 1.5-T MRI imaging system (Philips ACS-NT; Best; The Netherlands) with a maximum gradient amplitude of 23 milliTesla/meter and a rise time of 200 ms. To determine the exact circulation time of the contrast bolus from the injection site to the PAs, a dynamic, single-slice, axial, and subcostal views with the patient in the supine or left lateral positions. PA systolic pressure was calculated by adding the right atrial pressure, which was assumed to be 5 mm Hg in all cases, to the peak pressure difference between right ventricle and atrium (Dp). Dp was calculated from the continuous-wave Doppler signal of the TR gradient by the use of the simplified Bernoulli equation (Dp = 4v², where v is the peak flow velocity of the tricuspid regurgitant jet). The velocities in the tricuspid regurgitant jet were obtained from the apical four-chamber view. PAH was defined as a calculated PA systolic pressure of > 35 mm Hg.

Interpretation of MRI Images

All PMRA images were interpreted by an experienced radiologist who had no knowledge of the findings of the echocardiographic-Doppler study or of the clinical status of the patient.

The right PA diameter (RPAD) was measured at the widest portion that was distal to the bifurcation of the main PA. Measurements were performed manually on the MRI workstations by applying the integrating software.

The criteria for the diagnosis of chronic PAH by PMRA were the following: (1) dilated central PAs (RPAD, > 28 mm); and (2) an abnormal proximal-to-distal tapering of the PAs. The diagnostic criterion for acute and chronic PE was the presence of an intravascular filling defect.

Either conventional pulmonary angiography or spiral CT scanning was performed in all patients who had acute/subacute PE suspected by PMRA to confirm the diagnosis.

Statistical Analysis

The mean ± SD, sensitivity, specificity, and the positive and negative predictive values were calculated using standard epidemiologic formulas. Variables between groups were compared by unpaired t test. A p value < 0.05 was considered to be statistically significant.

Results

On the basis of patient history, Doppler echocardiography study, and either conventional pulmonary angiography or spiral CT scanning, 15 patients were found to have acute PEs, 18 patients were found to have chronic PAH (primary PAH, 4 patients; secondary PAH due to cardiomyopathy, 11 patients; chronic thromboembolic PAH, 2 patients; PA sarcoma, 1 patient), and 17 patients were found to have neither acute PE nor chronic PAH.

Echocardiographic Findings

Systolic PA pressure was found to be > 35 mm Hg in 27 patients by Doppler echocardiography. It was significantly higher in patients with chronic PAH (Fig 1) compared to patients with acute/subacute PEs (68 ± 25 vs 42 ± 23 mm Hg, respectively; p < 0.005). Only 60% of patients (9 of 15 patients) with acute PEs had a systolic PA pressure > 35 mm Hg. The mean systolic PA pressure in patients with acute/subacute PEs was significantly higher compared to patients without PAH (42 ± 23 vs 24 ± 4 mm Hg, respectively; p < 0.01).

PMRA Findings

PMRA correctly identified all 15 patients with acute/subacute PEs. Acute PE was differentiated from chronic PAH by the detection of intravascular filling defects. None of the patients with acute/subacute PEs showed abnormal proximal-to-distal
tapering of the PAs. An RPAD of > 28 mm as a sign of PAH was present in only three of nine patients (33%) with acute PEs.

Chronic PAH was correctly identified by PMRA in 16 of 18 patients (sensitivity, 89%). Fifteen of 18 patients (83%) with chronic PAH showed an RPAD of > 28 mm, and an abnormal proximal-to-distal tapering of PAs was present in 10 of 18 patients (56%). Two of the three patients with chronic PAH and an RPAD of < 28 mm had only moderate PAH.

All 17 patients without PAH had normal findings on PMRA (specificity, 100%). Only 1 of 18 patients with normal findings on PMRA had moderate chronic PAH (negative predictive value, 94%).

RPAD (Fig 2) was significantly greater in patients with acute PEs compared to patients without PAH (26.0 ± 3.1 vs 23.5 ± 2.8 mm, respectively; p < 0.05), but it was significantly smaller compared to patients with chronic PAH (29.6 ± 3.4 mm; p < 0.005).
Frequencies of the correct diagnoses of PAH and abnormal vessel findings based on PMRA are shown in Table 1.

**DISCUSSION**

**PAH**

PAH is an adverse sequela of many cardiac and respiratory conditions. With the exception of acute PE, PAH often develops insidiously, producing few diagnostic clues until chronic cor pulmonale becomes clinically evident. Therefore, it is important to rely on a diagnostic modality that allows an accurate determination of the presence and severity of PAH in patients with underlying cardiopulmonary disease. A study using PMRA in patients with different causes of PAH, including patients with acute PEs as well as chronic PAH, has not been reported.

We found that PMRA shows features that reliably distinguish patients with acute or subacute PEs from those with chronic PAH and from those without PAH or PE. The features seen by PMRA that reliably allowed the diagnosis of acute PAH due to PE were intravascular filling defects and a lack of abnormal proximal-to-distal tapering of the PAs. PMRA allowed an exact determination of the anatomic localization and extent of the PE in the central and segmental parts of the PA (Fig 3). Chronic PAH was correctly identified in 89% of our patients with the criteria of dilated central PAs (ie, RPAD $\geq 28$ mm) or abnormal proximal-to-distal tapering of the PAs (Fig 4). These findings are in agreement with a study by Bergin et al, who reported a comparable sensitivity (92%) of PMRA for the detection of chronic PAH due to chronic thromboembolic PAH or primary PAH. In our study, PMRA was highly specific (that is, no patient without PAH had abnormal findings on PMRA) and yielded a high negative predictive value (94%) for PAH.

Previous studies using CT scanning demonstrated that the diameter of the PAs is a strong predictor for the presence of PAH. Kuriyama et al$^6$ reported an upper limit of 28.6 mm for the diameter of the main PA in patients without PAH. He reported a diameter of $\geq 29$ mm on a CT scan to have a sensitivity of 69%

<table>
<thead>
<tr>
<th>PMRA findings</th>
<th>Acute PE (n = 15)</th>
<th>Chronic PAH (n = 18)</th>
<th>No PAH (n = 17)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intravascular filling defects</td>
<td>100 (15)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>RPAD $\geq 28$ mm</td>
<td>20 (3)</td>
<td>83 (15)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Abnormal proximal-to-distal tapering</td>
<td>0 (0)</td>
<td>56 (10)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Correct diagnosis (sensitivity)</td>
<td>100 (15)</td>
<td>89 (16)</td>
<td>100 (17)</td>
</tr>
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</table>

*Values given as % (No. of patients).
and a specificity of 100% for predicting PAH in patients with cardiopulmonary disease. Gunthaner et al7 measured the diameter of the main PA directly from contrast-enhanced CT images in healthy patients and in patients with well-documented cardiac pathology. They obtained a PA diameter of 28 mm as the upper limit for patients without PAH. However, this study included only a very small sample of 10 patients. There are only limited data on the use of PMRA with regard to PA diameters and the prevalence of PAH.8 In our study, all patients without PAH had an RPAD of <28 mm, resulting in a specificity of 100%. In the absence of chronic PAH, PAs were found to taper gradually, with the diameter of the proximal vessels being slightly larger than those of vessels in the peripheral third of the lung. Eighty-three percent of patients with chronic PAH showed an RPAD of >28 mm, whereas an abnormal proximal-to-distal tapering of PAs was present in only 56% of patients. Two of the three patients with chronic PAH and RPADs of <28 mm experienced only moderate PAH. However, in the case of PAH due to an acute PE, the RPAD was abnormal in only three of nine patients (33%).

PE

PE is a commonly encountered clinical problem that is potentially fatal. Due to the lack of specific signs or symptoms, its diagnosis relies on imaging techniques. Currently, pulmonary angiography is thought to be the “gold standard” for the diagnosis of PE. However, because of its invasive nature, it carries a 6% risk of morbidity and a 0.5% risk of mortality.8,9 Therefore, many physicians are reluctant to refer patients for pulmonary angiography, even if it is appropriate.

Ventilation-perfusion scintigraphy has found widespread application as a first-line imaging technique. However, although the technique is characterized by a very high sensitivity (98%), it also has a disappointingly low specificity (10%), as shown by the results of the Prospective Investigation of Pulmonary Embolism Diagnosis study.10 Furthermore, the results of ventilation-perfusion scintigraphy remain inconclusive for PE in most patients.

Recent improvements in MRI techniques have substantially increased the potential of MRI for the evaluation of pulmonary circulation. In contrast to ventilation-perfusion scintigraphy, MRI allows the identification and differentiation of pathologic conditions of the chest other than PE, which may account for the patients’ symptoms. PMRA is highly accurate in demonstrating central, lobar, and segmental PEs. Meaney et al12 compared PMRA to conventional pulmonary angiography in 30 patients with suspected PEs and identified all 5 lobar and 16 of 17 segmental PEs correctly with PMRA. In a study published in 1999 by Gupta et al,3 PMRA was also highly accurate in demonstrating lobar and segmental PEs. However, they were able to identify only one of five subsegmental PEs with PMRA.

PMRA has several advantages over spiral CT scanning. PMRA needs no iodinated contrast medium, with its risk of hypersensitivity and renal toxicity. The MRI contrast medium gadolinium is not nephrotoxic. Furthermore, PMRA needs no ionizing radiation. With respect to the peripheral lung perfusion, PMRA offers the ability to determine regional differences in perfusion, which is not possible with spiral CT scanning.

Further improvements in PMRA techniques are likely to lead to better results in the near future. Faster imaging techniques will allow shorter breathholds, which are necessary especially for patients with severe dyspnea.11 This will result in less severe motion artifacts. The potential use of blood pool agents holds promise with respect to better image quality.12 Refined MRI techniques will offer excellent spatial and temporal resolution for PMRA, which may soon rival conventional pulmonary angiography.

Limitations

Echocardiographic Doppler examinations were used to determine the presence of PAH. Several previous investigators reported very close correlations between the direct measurements of pulmonary arterial systolic pressure and noninvasive estimates based on continuous-wave Doppler measurements of the maximal tricuspid regurgitant jet velocity.1,13,14 We refrained from invasive right-heart catheterization in this study because we used a qualitative categorization of patients (patients with PAH vs those without PAH) who had no special need for exact hemodynamic measurements of the PA pressure. In all patients, the accurate evaluation of the TR for the calculation of PA systolic pressure was possible.

Conclusion

PMRA is a promising, safe, and accurate noninvasive imaging modality in patients with acute PEs. PEs can be visualized clearly as intravascular filling defects. Moreover, the PMRA technique might be considered to be a sensitive and highly specific screening tool in patients with suspected chronic PAH. The upper limit for a normal RPAD is 28 mm. This value is sensitive and highly specific for the prediction of chronic PAH.
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