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PULMONARY VASCULAR DISEASE

Magnetic Resonance Imaging of Pulmonary Embolism: Diagnostic Accuracy of Unenhanced MR and Influence in Mortality Rates

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Abstract
Objectives We evaluated the diagnostic value for pulmonary embolism (PE) of the True fast imaging with steady-state precession (TrueFISP) MRI, a method that allows the visualization of pulmonary vasculature without breath holding or intravenous contrast.
Methods This is a prospective investigation including 93 patients with suspected PE. All patients underwent TrueFISP MRI after undergoing CT pulmonary angiography (CTPA). Two independent readers evaluated each MR study, and consensus was obtained. CTPA results were analysed by a third independent reviewer and these results served as the reference standard. A fourth radiologist was responsible for evaluating if lesions found on MRI for both analysis were the same and if these were the correspondent lesions on the CTPA. Sensitivity, specificity, predictive values and accuracy were calculated. Evidence for death from PE within the 1-year follow-up was also assessed.
Results Two patients could not undergo the real-time MRI and were excluded from the study. PE prevalence was 22%. During the 1-year follow-up period, eight patients died, whereas PE was responsible for 12.5% of cases. Between patients who developed PE, only 5% died due to this condition. There were no differences between MR and CT embolism detection in these subjects. MR sequences had a sensitivity of 85%, specificity was 98.6% and accuracy was 95.6%. Agreement between readers was high ($\kappa = 0.87$).
Conclusions Compared with contrast-enhanced CT, unenhanced MR sequences demonstrate good accuracy and no differences in the mortality rates in 1 year were detected.

Keywords Pulmonary embolism · Magnetic resonance imaging · Computed tomography angiography · Mortality rate

Abbreviations

CTPA	Computed tomography pulmonary angiogram
PE	Pulmonary embolism
ROC	Receiver operating characteristic
RT-MRI	Real-time magnetic resonance imaging

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SD	Standard deviation
SSPE	Subsegmental pulmonary embolism
TE	Echo time
TR	Repetition time
TrueFISP	True fast imaging with steady-state precession

Introduction

Pulmonary embolism (PE) is a prevalent cardiovascular emergency that may lead to acute severe right ventricular failure by obstructing the pulmonary artery. Missed diagnosis, instead of treatment failure, is responsible for an overwhelming majority of deaths from PE [1]. Untreated mortality is estimated at 23–87%, whereas a mortality of 3–6% was found at 3 months following PE therapy [2]. In addition, post-mortem studies demonstrated that more than half the deceased patients due to PE were not suspected of having this condition while still alive [3]. Since its clinical manifestation is usually non-specific, imaging plays a fundamental role in the diagnosis of PE [4].

The multidetector computed tomography pulmonary angiogram (CTPA) is the current standard for imaging acute PE [5]. This test is available in many emergency departments, requires few seconds to be executed, and besides being capable of diagnosing a lethal condition, it can simultaneously exclude or recognize several differential diagnoses [6]. However, CTPA has intrinsic disadvantages, such as exposure to ionizing radiation and requirement of iodinated contrast media use. Radiation exposure is a concern because of its association with higher cancer risks, particularly in young and pregnant patients [7]. In the latter group, diagnosing PE accurately is even a greater challenge, as PE has a sixfold increased risk during pregnancy and is responsible for about 15% of maternal deaths in developed countries [8, 9]. In addition, CTPA is contraindicated in up to 22% of the patients because of renal insufficiency or allergy to iodine-based contrast media and contrast material-induced nephropathy following CT angiography should be a concern [10].

Alternative techniques have been evaluated for PE diagnosis. MRI, for example, achieved a performance close to CTPA, especially when combined techniques are used [1, 11–13]. Besides, it is a radiation-free imaging modality, and risks of complications from contrast agents are reduced, especially if unenhanced methods are used [14]. However, longer duration and the necessity of breath holding have been considered as main disadvantages of pulmonary MRI when compared with CT. Critically ill patients do not tolerate the breath-hold time needed for contrast-enhanced MR examinations and its imaging results might be suboptimal in these scenarios. For these reasons, True fast imaging with steady-state precession (TrueFISP) MRI may be a better approach for PE detection [15].

TrueFISP MRI allows the visualization of pulmonary vasculature without need for breath holding [16]. Besides, intravenous contrast material is not required, since intravascular clots can be visualized as signal voids within the spontaneous high signal intensity of the circulating blood in vessel lumens [13, 16]. Therefore, this prospective study was performed to appraise the diagnostic value of TrueFISP MRI in patients with suspected acute pulmonary embolism, in comparison with CTPA. Evidence for death from PE within the 1-year follow-up was also accessed.

Methods

Patients

The local ethics committee approved the prospective study, and written informed consent was obtained from all patients.

Ninety-three consecutive patients referred to the Radiology Department with clinical suspicion of acute PE were included in the study [59 women and 34 men; mean age of 63 years (SD ± 13; range 22–89)]. Patients initially underwent multidetector CT imaging to confirm the diagnosis and afterwards, without postponing medical treatment, underwent real-time MR imaging. Exclusion criteria were any contraindications to MRI examinations, such as claustrophobia or to iodinated contrast media.

One year after the CTPA and MR imaging, patients were reassessed through hospital records and mortality was registered.

Protocol

Computed tomography angiography was performed using a multidetector scanner (64-slice Light Speed VCT scanner, GE Healthcare Technologies, Waukesha, Wisconsin, United States of America), using the following scan parameters: 130 mAs, 120 kV, 0.6-mm collimation, 330-ms rotation speed, 1-mm reconstruction slice thickness and 0.75-mm reconstruction interval. Iodine contrast medium (370 mg iodine/mL; iopamidol 370, Bayer AG, Germany) was injected via the right antecubital vein at a rate of 5 ml/s with dose of 1.2 ml/kg. Image acquisition was started using a bolus-tracking technique (5 s after reaching a threshold of 120 HU in a region of interest within the main pulmonary artery).

The RT-MRI images were acquired on a 1.5-Tesla MR scanner (Magnetom AERA, Siemens Medical Solutions, Erlangen, Germany), using a true fast imaging with steady-state precession (TrueFISP) single-shot sequence, without cardiac gating, similar to techniques found in the literature [16]. The protocols used were adjusted for minimal time of acquisition and for high spatial resolution. An eight-channel body surface coil was adopted. The following parameters were used: TR (repetition time): 3.1 ms; TE (echo time): 1.5 ms; flip angle 60°; bandwidth 1000 Hz. 100 contiguous slices in the coronal plane were made using a field of view (FOV) of 360 mm, 256 × 192 matrix, slice thickness of 4 mm, 2-mm overlap and an acquisition time of 0.52 s per slice. 100 contiguous slices in the sagittal plane were made using a FOV of 360 mm, 256 × 180 matrix, slice thickness of 4 mm, 2-mm overlap and an acquisition time of 0.45 s per slice. 120 contiguous slices in the transverse plane were made using a FOV of 340 mm, 256 × 156 matrix, slice thickness of 3 mm, 1.5-mm overlap and an acquisition time of 0.4 s per slice.

Evaluation

All the MRI examinations were analysed independently by two radiologists, with 10 and 9 years of experience, blinded to the CTPA results, and a consensus was obtained for the final diagnosis. A third independent reader, with 25 years of experience, evaluated the CT images to avoid any recall bias. A fourth radiologist was responsible for evaluating whether the clots found on MRI for both analysis were the same and whether these were the correspondent lesions on the CTPA.

For the diagnosis of PE to be confirmed, concordant results from two planes were necessary and one of the following criterion: direct visualization of the thrombus; cut-off of pulmonary vessel; or any sudden changes in the signal intensity during the course of the pulmonary artery. The PE was graded in the same way for both examinations as central, lobar, segmental or subsegmental.

On the RT-MRI, the images were labelled according to their diagnostic quality and they were assumed as a non-diagnostic quality examination if more than three lobar arteries or more than half of the segmental arteries could not be identified or a blurred vascular representation could not exclude PE.

Statistical Analysis

The results of the MRI analysis were compared to the ones obtained from the CTPA, the gold standard imaging modality for pulmonary embolism. Initially we performed a patient-based analysis, comparing whether the patient had any emboli on both CT and MR images. Secondarily, we assessed MRI diagnostic performance according to each lesion. Sensitivity, specificity and positive and negative predictive values were calculated for the real-time MRI, and accuracy represented in a ROC (receiver operating characteristic) curve. The area under the curve was calculated, using a 95% confidence interval. We used the kappa statistic to evaluate the inter-radiologists agreement. Its interpretation was conducted based on the following parameters: kappa < 0.20, poor agreement; kappa = 0.21–0.40, fair agreement; kappa = 0.41–0.60, moderate agreement; kappa = 0.61–0.80, good agreement; kappa = 0.81–1.00, very good agreement [17]. All the results were statistically analysed using the software Stata, version 11 (StataCorp, College Station, TX, USA).

Results

The multidetector CT examinations were performed in all the 93 patients. Two subjects could not finish the RT-MRI due to phobia and were excluded from the study. Diagnostic quality was obtained in all the MRI exams for the remaining 91 patients.

The complete imaging protocol for RT-MRI took a median of 8 min (SD ± 3.2 min) to be performed. The time interval for repositioning the patient from bed to the magnet and back has not been assessed. The PE was confirmed in 20 of 91 patients (22%), accepting the multidetector CT as the reference standard modality for the diagnosis. Among these patients, considering the possibility of emboli in different levels in the same subject, 30% ($n = 6$) had emboli in the pulmonary trunk, 40% ($n = 8$) in lobar arteries, 35% ($n = 7$) in the segmental level and 30% ($n = 6$) were subsegmental PE (SSPE) (Table 1). Isolated SSPE represented 10% of the PE cases ($n = 2$).

Figure 1 demonstrates PE in the left lower lobe artery in a 23-year-old woman with chest pain and dyspnoea, comparing the contrast-enhanced CTPA and the real-time MRI in the transverse and sagittal views.

Per-patient Analysis

MR imaging showed four false-positive findings, all within the lingula, in patients from 81 to 88 years old, that were considered as segmental PE due to sudden changes in the signal intensity of the corresponding lingular arteries. In addition, one patient was considered as a false-negative result due to a subsegmental embolism in the right lower lobe. Sensitivity for this modality was 85% and specificity, 98.6%. Positive predictive value was 94.5%, negative predictive value, 95.9% and the accuracy for the RT-MRI, 95.6% (Table 1). The area under the ROC curve was 0.956 (95% confidence interval: 0.891–1.000). A good inter-reader agreement was obtained for the MRI ($\kappa = 0.87$).

Table 1 Pulmonary emboli prevalence and location and RT-MRI diagnostic performance

Prevalence	20 (22)
Location	
Pulmonary trunk	6 (30)
Lobar arteries	8 (40)
Segmental arteries	6 (30)
Subsegmental arteries	6 (30)
MRI Diagnostic Performance	
Per-patient analysis	
Sensitivity	85.0%
Specificity	98.6%
PPV	94.5%
NPV	95.9%
Accuracy	95.6%
AUC†	0.956 (0.891–1.000)
Per-embolus analysis	
Sensitivity	85.0%
Specificity	95.8%
PPV	85.0%
NPV	95.8%
Accuracy	94.5%
AUC†	0.934 (0.841–1.000)

Note—*AUC* area under the curve, *NPV* negative predictive value, *PPV* positive predictive value, *RT-MRI* real-time magnetic resonance imaging

Data are number of patients and percentages are in parenthesis

†Data in parenthesis are 95% confidence intervals

Per-embolus Analysis

In the secondary analysis, comparing each lesion individually on CT and MRI, the same three false-positive findings were identified, all within the lingula. In addition, three false-negative results were found. One was the subsegmental clot in the right lower lobe also described at the per-patient analysis. The other two, a segmental embolus in the left lower lobe and a subsegmental in the right lower lobe, were considered as true-positive results in the initial analysis, as they had other clots in different arterial levels that could be visualized on both imaging modalities. After the per-embolus analysis, MRI diagnostic performance slightly decreased. Sensitivity was 85% and specificity, 95.8%. Positive predictive value was 85%, negative predictive value, 95.8% and the accuracy for the RT-MRI, 94.5% (Table 1). The area under the ROC curve was 0.934 (95% confidence interval: 0.841–1.000).

Mortality

After the period of 1 year, reassessing the hospital records revealed a mortality rate of eight patients (8.79%), due to cerebral metastasis ($n=3$), myocardial infarction ($n=2$), pulmonary infection and sepsis ($n=1$), automobile accident ($n=1$) and PE complications ($n=1$). Among these patients, there was no difference between the CTPA and the RT-MRI findings.

Discussion

Free-breathing TrueFISP sequence is an alternative technique for the use of MRI in the diagnosis of acute PE. Different from other imaging methods, such as MRA, contrast material administration is not necessary, the resistance to motion degradation allows imaging in patients who are incapable of successful breath holding, and there is visualization of the vessel wall, allowing circumscribed visualization of a partial embolus [14].

Prior studies that also considered the CTPA as the reference standard reported high specificity and high inter-reader agreement for this unenhanced MRI technique, ranging from 94.5 to 100% and from 0.62 to 0.93, respectively [12–14]. Likewise, in our study, we found high specificity (98.6%) of TrueFISP MRI in comparison with CTPA, additionally suggesting a positive finding sufficient to initiate anticoagulation. In addition, a very good inter-reader agreement was found ($\kappa = 0.87$), as well as high global sensitivity of the technique (85%). After comparing each lesion individually, MRI diagnostic performance slightly decreased, but maintained high (accuracy at per-patient analysis, 95.6%; accuracy at per-embolus analysis, 94.5%). Different from the other reports, our study focused primarily on a per-patient analysis rather than per-embolus, an approach that might be more relevant to clinical practice. Our sample also differed from the ones previously reported as patients were from a granulomatous disease-endemic region, where reticular opacities and mediastinal fibrosis are more prevalent and could create a higher rate of false-positive results.

Although global sensitivity was high, it became lower as pulmonary arteries extended distally, with lobar PE representing 70% of PE found. When the thrombus was within a central or lobar level, its detection was easier, as a direct visualization was possible. At the segmental level, thrombus detection demanded more time, as images were analysed in the axial, coronal and sagittal planes to achieve more diagnostic certainty. Kluge et al. [16] had previously demonstrated that RT-MRI was less sensitive than MR perfusion in detecting subsegmental embolism. Hosch et al. [12] reported decrease of both sensitivity and specificity of combined MRI techniques when the location of embolic material was peripheral. In addition, Revel and colleagues [13] reported that, when excluding PE limited to the segmental or subsegmental levels, the sensitivity of unenhanced MRI sequences reached 100%.

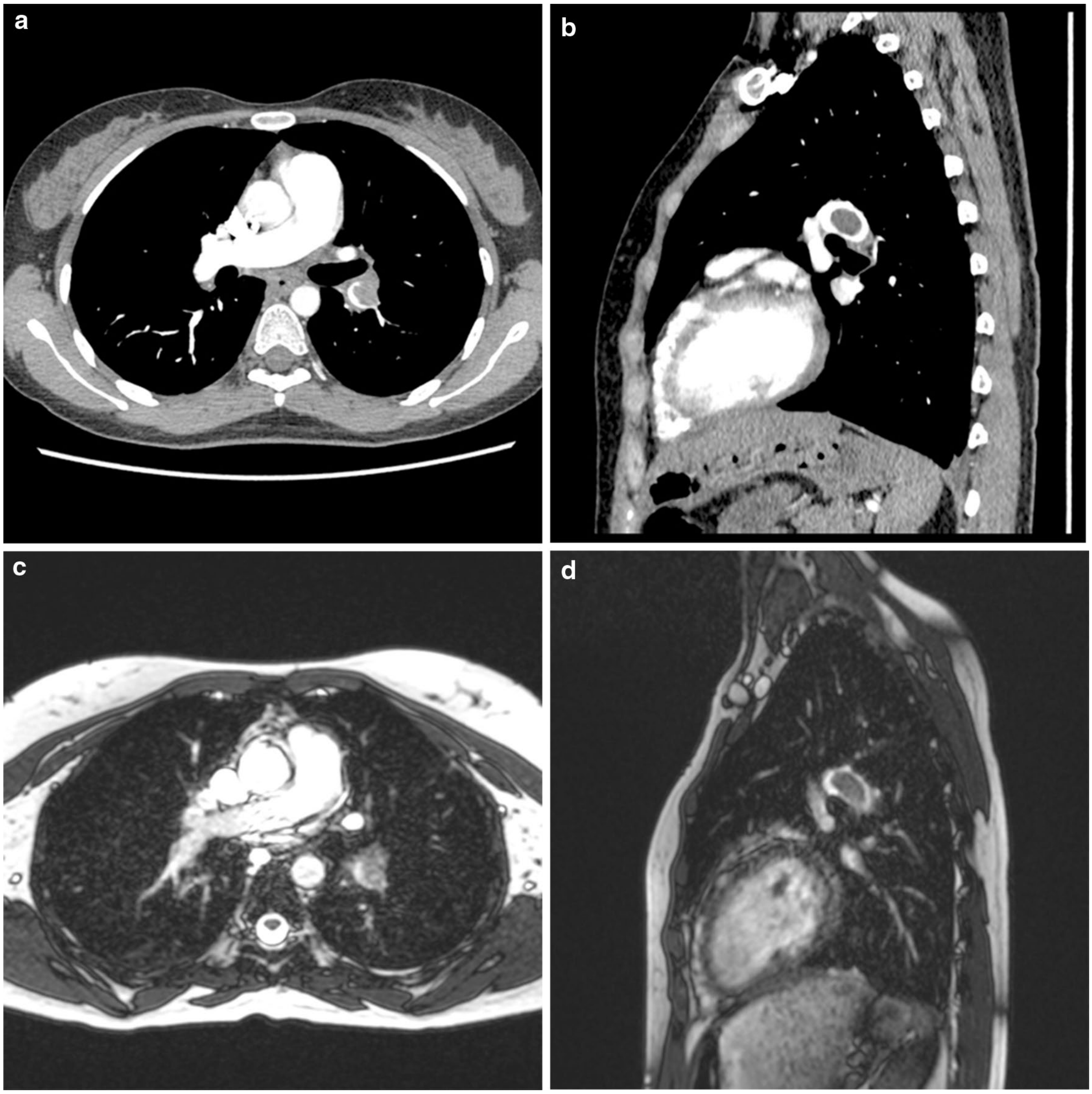

Fig. 1 A 23-year-old woman with chest pain and dyspnoea. **a** Contrast-enhanced CTPA dataset demonstrated PE in left lower lobe artery in the transversal and **b** sagittal views. **c** Real-time TrueFISP dataset in corresponding transversal and **d** sagittal views

Nevertheless, reports of increased PE incidence with minimal change in overall mortality lead to the debate about the importance of detection of small emboli reached by CT. Burge et al. found that the number of patients with a primary diagnosis of PE nearly doubled over the 11-year study period, during a time of widespread use of CT. However, PE deaths did not vary significantly—from 157 to 159 over the same period [18]. Besides, the management of isolated subsegmental PE without a deep venous thrombosis is still controversial, as the use of an anticoagulant therapy may not overweight its risks. Pena et al., reassessing their data covering 4410 CTPA exams, found that out of the 18 patients with SSPE not treated with anticoagulation (14 single SSPE and 4 multiple SSPE), none suffered from a subsequent VTE in the 3-month follow-up period [19]. In a Cochrane systematic review, Yoo et al. found no randomized controlled trial evidence for the effectiveness and safety of anticoagulation therapy versus no intervention in patients with isolated SSPE or incidental SSPE [20].

Another point that supports the use of TrueFISP MRI is the lack of differences between the CTPA and the RT-MRI findings for the deceased patients. This suggests that unenhanced MR imaging was as capable as the CT pulmonary angiography in detecting more life-threatening conditions. Besides, it also raises suspicion concerning the clinical meaning of distal emboli, as the only false-negative case reported in our study was due to a SSPE.

Regarding the false-positive findings, all the cases found in this study were related to segmental emboli in the lingula. Prior studies also reported inferior results when investigating PE with RT-MRI in this segment, compared to other parts of the lung [14]. This is possibly due to the vascular geometry in the lingula, in addition to motion effects. All false-positive cases were elderly patients, which might be related to less compliance for performing the examinations. Further studies should try to compare RT-MRI diagnostic performance separating subjects according to their age. Further refinements in MRI techniques, specially focused on spatial resolution and edge sharpness, might reduce these false-positive and false-negative rates.

As the CTPA, real-time MRI also allows diagnosing accurately coincidental findings, such as pleural and pericardial fluid collection, aortic dissection and pulmonary opacities, aspiration, atelectasis or bleeding, an advantage over other modalities, such as scintigraphy and pulmonary angiography [16, 21–23]. Considering the short examination time compared to other MRI modalities, another advantage of the TrueFISP technique is the possibility of repeating the acquisitions if the results are inconclusive.

One of the limitations of this study was the lack of additional examinations to confirm the initial suspicion of PE, such as D-dimer tests, echocardiography and duplex phlebosonography, which could lead to an underestimated PE prevalence. However, the prevalence found in this study (22%) is comparable to previous CTPA series [13]. Another limitation is that this is a single-centre study, which could limit the accuracy of the results, however, this also increases the homogeneity of the technical parameters.

PE was responsible for 12.5% of all deaths registered 1 year later (1 of 8), whereas only 5% of patients who developed this condition died due to PE. These rates are similar to those described in previous studies. Donze et al. [2] reported a mortality of 3–6% at 3 months following PE therapy and Janata et al. [24] described mortality rates of 15% for overall analysis and 1–2% for patients who were stable enough to undergo diagnostic procedures as CT and ventilation/perfusion lung scintigraphy (V/Q-Scan). Further studies should try to investigate the risk of mortality from PE with the cardiac index right ventricle / left ventricle, maybe comparing its usefulness in each imaging modality.

Conclusions

Our results additionally suggest real-time MRI as being a useful tool for establishing the diagnosis of acute PE in central pulmonary vessels. Compared with contrast-enhanced CT, unenhanced MR sequences demonstrate good accuracy and no differences in the 1-year mortality rates.

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Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. ISCMPA Committee (Porto Alegre, Brazil).

Informed Consent Informed consent was obtained from all individual participants included in the study.

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