Original Article
Diagnostic value of three-dimensional contrast-enhanced MR pulmonary angiography with liver acquisition volume acceleration sequence on a 3-T MR system for acute pulmonary embolism

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Abstract: To assess the value of three-dimensional (3D) contrast-enhanced (CE) magnetic resonance pulmonary angiography (MRPA) with liver acceleration volume acquisition (LAVA) in the detection of acute pulmonary embolism (PE). Thirty-two patients with symptoms indicative of acute PE underwent both CT pulmonary angiography (CTPA) and MRPA within 4 hours. Three of the patients were excluded from the final analysis. The results of MRPA were compared with those of 256-slice CTPA, which served as the reference standard. The pulmonary emboli were independently analyzed on per-patient and per-vascular zone bases by two radiologists in consensus. The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) for PE detection were calculated. Twenty-three patients had PEs which were observed in 3 of the 46 main arteries, 22 of 138 lobar arteries, and 38 of 414 segmental arteries on CTPA, and no PEs were detected in six patients. The readers correctly detected 59 clots in 22 patients using MRPA. The sensitivities, specificities, and NPVs for MRPA were 95.7%, 100% and 85.7% per-patient, respectively, 100%, 100% and 100% for the main PA, respectively, 95.4%, 100% and 99.3% for the lobar PA, respectively, and 86.8%, 100% and 98.9% for the segmental PA, respectively. The PPV was 100%. 3D contrast-enhanced MRPA on a 3-T MR system with a LAVA sequence is a suitable alternative modality to CTPA for the detection of PE on per-patient and per-vascular bases according to this small cohort study.

Keywords: three-dimensional magnetic resonance pulmonary angiography, LAVA, 256-slice computed tomography, acute pulmonary embolism

Introduction

Acute PE (APE) can be rapidly fatal and is considered the third most common acute cardiovascular disease after myocardial infarction and stroke [1]. If untreated, pulmonary embolism has an estimated mortality rate of 30%, which is 10 times higher than the annual mortality rate for treated pulmonary embolism (2.5%) [2]. Imaging has been assumed to have a pivotal role in the diagnosis of acute PE. Multidetector computed tomography (MDCT) angiography is currently accepted as the primary imaging modality and has sensitivities and specificities for the detection of PE that range from 83%-100% and 89%-97%, respectively [3-5]. However, MDCT has the inherent limitation of the radiation dose and the side effects of iodinated contrast material [6, 7], especially for younger individuals and female patients [8]. Therefore, an alternative test that requires no risks of exposure to ionizing radiation or iodinated contrast material for the detection of pulmonary embolism would be highly beneficial, given it has sufficient effectiveness.

Compared with CTPA, gadolinium-enhanced magnetic resonance angiography has attractive potential for the detection of APE, and it is free from ionizing radiation and the adverse

reactions to iodinated contrast, especially when non-enhanced MRI modalities are applied [9, 10]. Liver acceleration volume acquisition (LAVA) is a new versatile high-resolution angiography technique that provides improved diagnostic high-resolution imaging scans at much faster speeds. To the best of our knowledge, at present, no reports have been published to validate the diagnostic accuracy of MRPA with LAVA in the detection of PE using a 3-T MR system. Therefore, the purposes of this prospective study were to evaluate whether 3D contrast-enhanced MRPA on a 3-T system with LAVA could be used as a reliable alternative diagnostic test for PE; 256-slice CTPA was used as the reference standard and to decrease the rate of technically inadequate studies.

Material and methods

Patients

This prospective study was approved by the local ethics committee, and informed written consent was obtained from all patients. A total of 32 consecutive patients (21 males and 11 females, age range 30-74 years, mean age, 55 years) were included in this study. The patients were inpatients (from the emergency department, respiratory internal medicine department, cardiovascular medicine department, department of wound orthopedics and the chest surgery department). APE was suspected if there was a combination of clinical symptoms (e.g., chest pain, sudden shortness of breath, hydrothorax, hemoptysis and hydroncus in both lower limbs), and the D-dimer level was >500 μg/l on an ELISA-based test (VIDAS, BioMérieux, Lyon France). The exclusion criteria were the following: age (below 18 years old); reported contraindication to iodi-nated contrast material; pregnancy; right heart strain; contraindication for MRI, including claustrophobia, a metallic ocular implant or a pace maker; reported contraindication to iodinated or gadolinium-based contrast agents; a glomerular filtration rate under 30 ml min^{-1}. 1.73 m^{-2}; and the inability to breath hold over 13 seconds. A patient body mass index above 30 kg m^{-2} was added as exclusion criteria due to difficulties encountered in performing MRI with obese patients. Contraindications also included dependency on a continuous connection to an external electrical device or pump.

Imaging protocol

CT pulmonary angiography: The imaging protocol used in the study was the standard PE protocol. Axial section images were examined. All patients underwent CTPA on a 256-slice CT scanner (Brilliance CT scanner, Philips Healthcare). All patients were placed in a supine position for scanning with their hands over their heads. The lungs were scanned from 2 cm above the aorta to the dome of right diaphragm. The scanning parameters included a 128 × 0.625 mm collimation, 0.625-mm thickness, iDose 4 reconstruction, a tube voltage of 80 kv, a rotation time of 0.5 seconds, a field of view (FOV) of 350 × 350 mm, and a matrix of 512 × 512. Automated tube current modulation was used in all CT studies (CARE Dose 4D, Siemens). Contrast-enhanced CT was routinely performed for all subjects in the mode and was obtained after the injection of a bolus of 50 ml of Ultravist (370 mg I/ml, Bayer Schering Pharma, Berlin, Germany) followed by 50 ml of saline solution into an antecubital vein (left first) via a 20-gauge injector (CT Injector Missouri, Ulrich Medical) with injection rate 5.0 ml/sec. Using a bolus tracking technique, a region of interest was placed into the superior vena cava, and image acquisition began after the region of interest reached the predefined threshold of 100 Hounsfield Units (HU). The scan took approximately 2.5 seconds.

Three-dimensional contrast-enhanced MRPA: MRPA was performed within 4 hours of CTPA on a 3-T unit (Signa HDxt system, GE Healthcare, Chalfont St Giles, UK) without any delay in medical treatment. Before undergoing MRPA, the patients were carefully instructed on breath-holding and practiced the technique to produce precisely the same degree of inspiration for each scanning series. The patient was positioned in a supine position with their hands on their head. An ECG signal was continuously monitored during the MR image acquisition. A specialized multichannel phased array surface coil (8 channels) was placed over the chest to receive the pulmonary MRI data.

First, an unenhanced coronal MRPA was obtained with the LAVA sequence in the axial plane with the following parameters: TR 3.3 ms, TE 1.5 ms, flip angle 12°, matrix 288 × 224, FOV 350 × 350 mm, acceleration factor 0.72, bandwidth 83.3 kHz pixel^{-1}, slice thick-

ness 4 mm, and overlap -2.0 mm. Optimal pulmonary arterial enhancement was determined using the test bolus technique. An intravenous injection of 20 ml of gadobenate dimeglumine with the flow rate of 2.0 ml/sec. was performed during dynamic scans at the level of the pulmonary trunk with a scan delay of 1 second. A region of interest as large as the pulmonary trunk was drawn and used to generate the enhancement curve. The time to peak enhancement was regarded as the optimal delay time for MRPA. Next, a dose of contrast of 0.1 mmol kg^{-1} body weight was injected using an automatic injector via a 24-gauge catheter powered by a MR injection system (Spectris Solaris EP, MR Injection System, Medrad, Germany) at a rate of 2.0 ml/sec. and followed by a saline flush of 20 ml at the same rate. A breath-hold 3D high-resolution MRPA in the axial plane and one in the coronal with LAVA sequence were then acquired using the same parameters as above. The scan time for the MRPA was less than 13 seconds.

Image analysis

All of the data including the CTPA and MRPA data were transmitted to the picture archiving and communication system (PACS) AW4.3 (GE Medical Systems, USA). The data sets from the CT and MR examinations were anonymous and were evaluated in a standardized manner with individually adapted window settings. Both lung and soft-tissue windows were used to identify the pulmonary arteries and bronchi. Reformations on sagittal and coronal slices were performedto visualize the pulmonary emboli if necessary. The diagnostic criteria for acute PE included the following: first, complete arterial occlusion with failure to opacify the entire lumen on more than one image in each of two planes with or without an artery that was enlarged compared with the pulmonary arteries of the same order of branching; second, a central arterial filling defect surrounded by intravenous contrast material; and third, a peripheral intra-luminal filling defect that made an acute angle with the arterial wall [11]. Vessel visualization was graded as non-diagnostic if a vessel could not be identified or if blurred vessel representation precluded analysis. The entire sequence was classified as non-diagnostic if more than three lobar arteries or more than 10 segmental arteries were not assessed with the sequence.

For statistical convenience, the pulmonary emboli were recorded as being present or absent in each of the following lung lobes: right upper lobe, right middle lobe, right lower lobe, left upper lobe, lingual area, and left lower lobe. If a pulmonary embolus was located in the bifurcation of the pulmonary artery, the most extensively involved pulmonary artery was noted [12]. The numbers of pulmonary emboli were also counted. Continuous filling defects that extended into branching vessels were regarded as single PEs at the location. Subsegmental emboli were not counted on either the CTPA or MRPA. The diagnosis of PE was made by the consensus of the two senior-attending radiologists (Honglun Li and Guangbin Wang) who have 15 and 22 years of experience, respectively, in interpreting CTPA and MRPA images. The images were selected in random order. These authors recorded the presence, numbers and locations of the PEs according to the above-mentioned methods. Additionally, to avoid any recall bias, the MR images were interpreted first, and the CTPA images were evaluated at least 4 weeks after MRI in a random manner. The CTPA results were regarded as the reference standard for PE detection. The level of PE was graded as main (two arteries per patient), lobar (six arteries per patient), or segmental (18 arteries per patient).

Statistical analysis

The statistical analyses were performed using the SPSS version 16.0 software (SPSS Inc. Chicago III, USA). The data was analyzed by chi-square.Using the CTPA as the reference standard, the diagnostic sensitivity, specificity, the positive predictive value (PPV) and the negative predictive value (NPV) of the MRPA for PE detection were calculated on per-patient and per-vascular zone bases at different pulmonary artery levels.

Results

All CTPA examinations were successfully completed without any observable adverse effects. Of the 32 patients with MRPA examinations, 3 patients were excluded from the final analysis for the following reasons: contrast agent leakage in one patient and failure of breath-hold cooperation in two patients. A total of 29 patients were included in the final analysis, of which 23 patients (79%) were diagnosed with

Table 1. Diagnostic value of MRPA for the detection of pulmonary embolism according to pulmonary vascular zone and per-patient

	Right Pulmonary				Left Pulmonary				Main	Lobar	Segmental	Person
	Right Pulmonary Artery	Upper Lobe	Middle Lobe	Lower Lobe	Left Pulmonary Artery	Upper Lobe	Lingula	Lower Lobe				
MRA	2	8	7	18	1	7	3	13	3	21	33	22
CTA	2	11	7	18	1	8	5	13	3	22	38	23
TP	2	8	7	18	1	7	3	13	3	21	33	22
TN	27	18	22	11	28	21	24	16	26	152	484	6
FP	0	0	0	0	0	0	0	0	0	0	0	0
FN	0	3	0	0	0	1	2	0	0	1	5	1
Sens. %	100 (2/2)	72.7 (8/11)	100 (7/7)	100 (18/18)	100 (1/1)	87.5 (7/8)	60 (3/5)	100 (13/13)	100 (3/3)	95.4 (21/22)	86.8 (33/38)	95.7 (22/23)
Spec. %	100 (27/27)	100 (18/18)	100 (22/22)	100 (11/11)	100 (28/28)	100 (18/18)	100 (24/24)	100 (16/16)	100 (27/27)	100 (152/152)	100 (484/484)	100 (22/22)
PPV, %	100 (2/2)	100 (8/8)	100 (7/7)	100 (18/18)	100 (1/1)	100 (7/7)	100 (3/3)	100 (13/13)	100 (3/3)	100 (21/21)	100 (38/38)	100 (22/22)
NPV, %	100 (27/27)	100 (21/21)	100 (22/22)	100 (11/11)	100 (28/28)	95.4 (21/22)	92.3 (24/26)	100 (16/16)	100 (27/27)	99.3 (152/153)	98.9 (484/489)	85.7 (6/7)

Note: TP = true-positive results; TN = true-negative results; FP = false-positive results; FN = false-negative results; Sens. = sensitivity; Spec. = specificity; NPV = negative predictive value; PPV = positive predictive value.
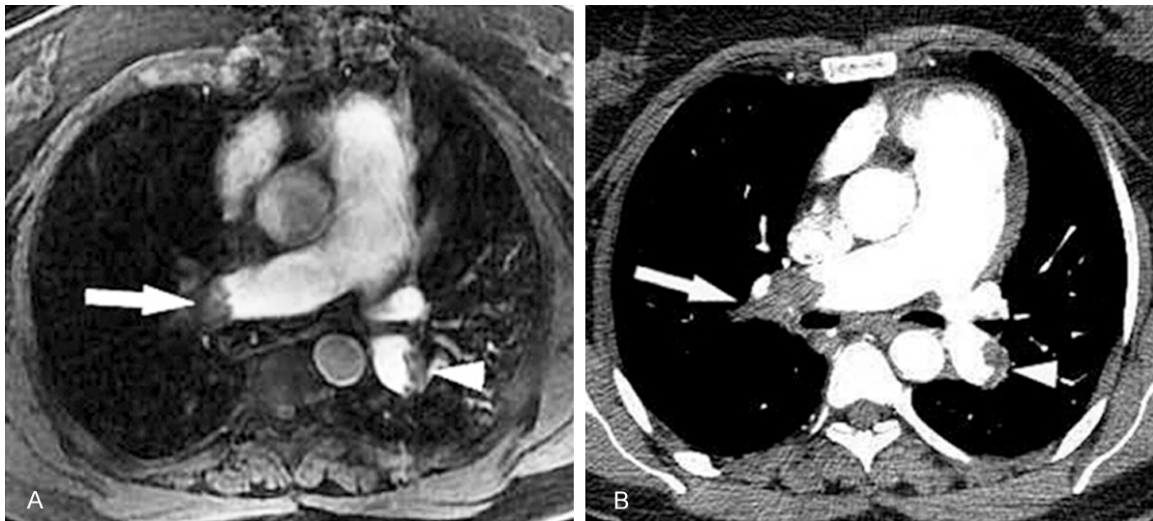
Figure 1. Woman, 46 years old, right pulmonary artery (arrow) and left lower lobar (arrowhead) embolism in CTPA (B) and CE-MRPA (A) image in axial.
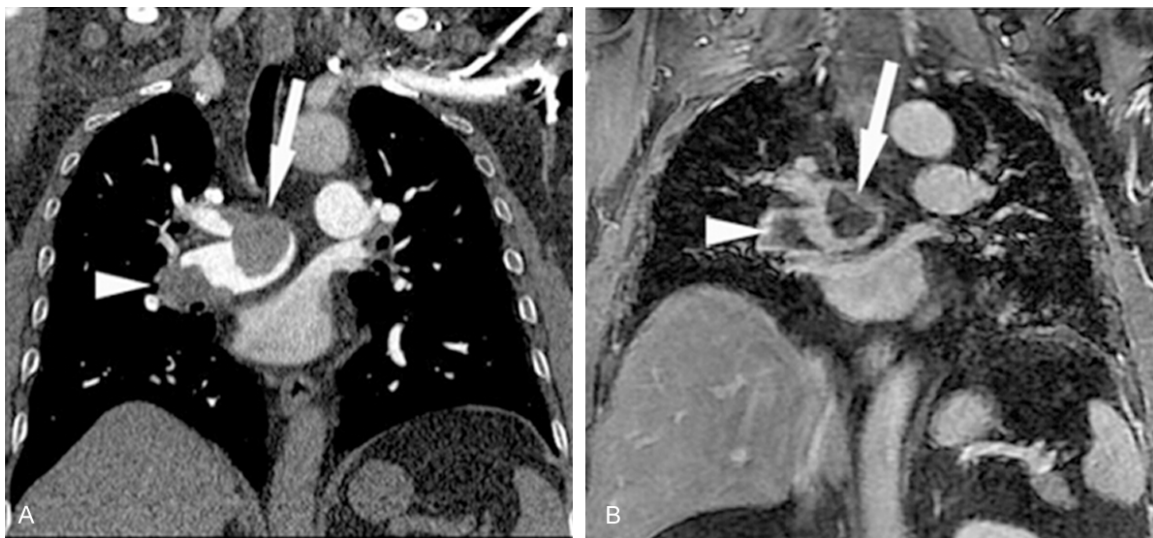

Figure 2. Man, 48 years old, right pulmonary artery (long arrow and arrowhead) embolism, in CTPA (A) and CE-MRPA (B) image in coronal.

63 pulmonary emboli on CTPA. Among these 23 patients, pulmonary emboli were observed in 3 of 46 main arteries, 22 of 138 lobar arteries, and 38 of 414 segmental arteries on CTPA. Of 63 total pulmonary emboli detected on CTPA, 59 pulmonary emboli in 22 patients were detected on the MRPA examinations. The results of the MRPA imaging interpretations categorized by vascular distribution and the statistics of the MRA detections of the pulmonary emboli on per-patient and per-vascular bases were summarized in **Table 1** using CTPA as the reference standard. No false-positive results were identified on MRPA. The sensitivities, specificities, and negative predictive values of MRPA were 95.7%, 100%, and 85.7% on the per-patient basis, respectively, 100%, 100%, and 100% for the main PA, respectively, 95.4%, 100%, and 99.3% for the lobar PA, respectively, and 86.8%, 100%, and 98.9% for the segmental PA, respectively. The positive predictive value was 100% (**Table 1**). One lobar and five segmental emboli were missed on MRI. Typical cases are illustrated in **Figure 1** (in the main and lobar PA), **Figure 2** (in the main PA), and **Figure 3** (in the segmental PA).
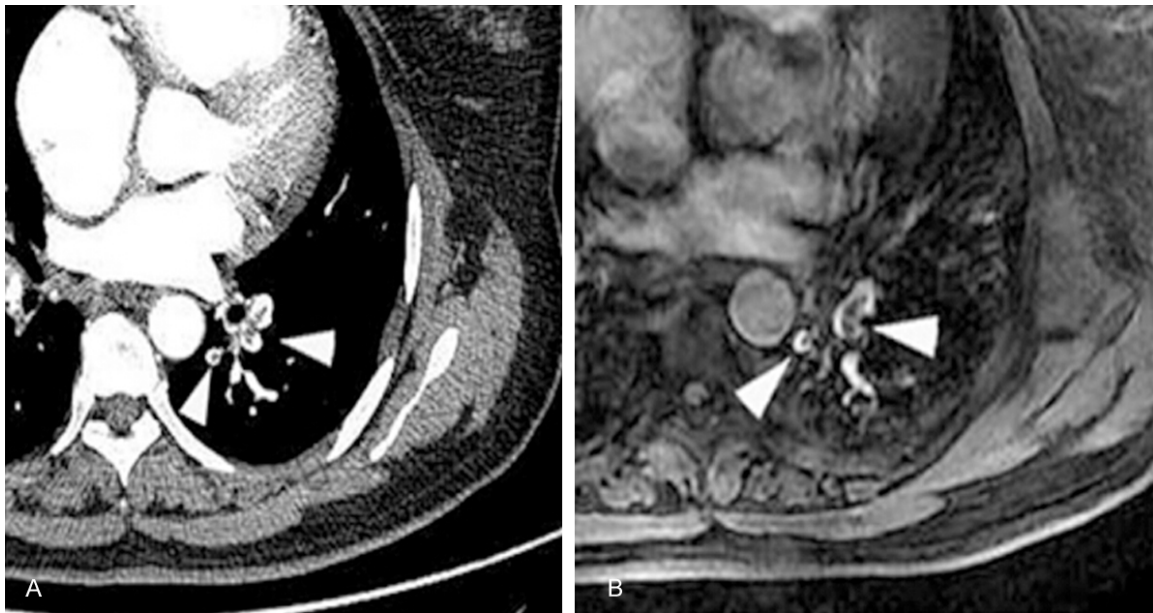
Figure 3. Man, 57 years old, left lower lobar segmental (arrowhead) embolism in CTPA (A) and CE-MRPA (B) image in axial.

Discussion

Our study revealed that the 3D contrast-enhanced 3 T MRPA with the LAVA sequence exhibited high sensitivity and specificity in the detection of main, lobar and segmental acute PEs in the hands of highly experienced radiologists in a small cohort study. Moreover, the examination time was short compared with 256-slice CTPA. This technique is a promising prospect as a primary noninvasive imaging modality for acute PE detection.

The PIOPED III study (the first large series evaluating MRI with confirmed or excluded PE) indicated a sensitivity that ranged between 45% and 100% at different centers and an average sensitivity of 78%, but the proportion of technically inadequate images ranged from 11% to 52% across the various centers [13]. Thus, it is necessary to optimize MRPA procedures to improve PE detection.

In the previous section, several modifications were demonstrated. The first modification was the use of different MR systems (1.5 T at only one center vs. 3 T). Patient subgroup analysis in a recently published PIOPED III study revealed that the 3-T MRPA protocol achieved higher spatial resolution yet maintained a significantly higher signal-to-noise ratio (≥13%, P = 0.03) in

the main pulmonary vessels relative to 1.5-T MRPA [14]. Recently, Zhang et al [12] validated the diagnostic accuracy of MRPA in the detection of PE using a 3-T MR system and found sensitivities of MRPA of 85.5% and 83.6%, 100% specificity, 100% PPV and high accuracy on a per-lobe analysis. Thus, the high technical success rate in our study is attributable to the use of a 3-T MR system.

The second modification was the use of a different dose of contrast medium (0.2 mmol/kg vs. 0.1 mmol/kg). In the latter study, Bueltmann et al [15] similarly demonstrated the significant qualitative and quantitative superiority of the 0.1 mmol/kg gadobenate dimeglumine dose relative to a similar dose of gadopentate dimeglumine on CE-MRA for the entire supra-aortic vasculature. The smaller dose (0.1 mmol/kg) is also associated with a lower risk of developing contrast-induced nephropathy.

The third modification was the reduced time taken for the acquisition and breath holding (14-22 seconds vs. 13 seconds). Motion artifacts are well known as the material cause that limits the use of MRI. Motion artifacts, usually due to respiratory motion, can substantially degrade image quality. This can be minimized by either rapid image acquisition or breath holding. In many previous studies the scan

time was 18-22 seconds [16], which is too long for many symptomatic patients to hold their breath. In our study, the breath-holding time for the patients was under 13 seconds; all of the patients were able to cooperate well, and excellent image quality was achieved.

The fourth modification was the use of a different fast scanning technique, i.e., LAVA. LAVA is a 3D spoiled gradient echo technology based on ASSET that involves segmented k-space techniques along the Z-axis, which further shortens the scanning time. Compared with the previous multiphase dynamic enhancement scanning technology of the abdomen, the scanning speed, the spatial resolution and the scanning range are improved by approximately 25%. Additionally, LAVA has a significant advantage in the new fat suppression technique for lesions and the surrounding tissue, whose k-space filling at slice selection adopts a partial zero-filling methodology and uses small-angle special inversion pulses to segment the signal acquisition. This process optimized the time for fat suppression inversion recovery at the center of the k-space and presents a symmetrical distribution, which greatly improves the fat suppression effect and provides a uniform fat suppression signal in addition to decreasing artifacts and the effect of edge enhancement [17]. Thus, the improvement in LAVA time resolution with the acquisition of the serial three-dimensional volume with thinner slices increases the detection rate of small lesions. Furthermore, the vessel walls can be visualized, which provides contrast outlining the intraluminal PE that is superior to that of conventional MRPA [18].

In our study, the sensitivities and specificities were 95.7% and 100% per person, respectively; 100% and 100% for the main PA, respectively; 95.4% and 100% for the lobar PA, respectively; and 86.8% and 100% for the segmental PA, respectively; and these values are higher than those of most of the public studies [19]. These differences can be attributed to the high-field MRI system, which improves the spatial resolution of MRPA and the fast scanning technique (LAVA). Our reported sensitivities of MRPA for PE detection are similar to those of Waldemar *et al* [20]; however, their MR system was 1.5 T, and the acquisition time was 22 seconds.

Although isolated sub-segmental PE has been reported in 4%-22% patients with suspected PE, most emboli were located in the main, lobar, and segmental arteries, and the present data provide evidence that an increase in the number of patients diagnosed with PE is not associated with PE mortality [21]. The clinical significance of sub-segmental pulmonary embolism (SSPE) is still unclear. Recently, some authors [22-24] have challenged the necessity of treating all SSPEs with anticoagulation. Multiple-detector CTPA seems to increase the proportion of patients diagnosed with SSPE without lowering the 3-month risk of thromboembolism, which suggests that SSPE might not be clinically relevant. There is no randomized controlled trial evidence for the effectiveness and safety of anticoagulation therapy versus no intervention in patients with isolated or incidental SSPE [24]. MRPA might be more than adequate for the detection of clinically significant emboli that require anticoagulation [16, 23]. We therefore limited the evaluations in our study to the clinically relevant main, lobar and segmental levels.

There are also some weaknesses in our study. This study was a single-center study, which might limit the reliability of our results. Further studies with larger cohorts of patients are needed. Second, there was a time delay of 4 hours on average between CTPA and MRPA. During that interval, all PE patients had begun receiving anticoagulation therapy. Thus, it is possible that some PEs could have been diminished by the time of the MRPA.

Our preliminary work suggests that contrast-enhanced 3-T MRPA with the 3D LAVA technique provides high-resolution multidirectional images of pulmonary arteries. Moreover, this technique appears to be an effective MRI sequence for diagnosing PEs in the main, lobar, and segmental pulmonary arteries on a per-patient basis and provides a potential diagnostic alternative to CTPA that does not involve the risks associated with exposure to ionizing radiation or iodinated contrast material.

Disclosure of conflict of interest

None.

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