Diagnostic accuracy of true fast imaging with steady-state precession, MR pulmonary angiography and volume-interpolated body examination for pulmonary embolism compared with CT pulmonary angiography

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Abstract. The diagnostic performance of magnetic resonance (MR) sequences for displaying different levels of pulmonary artery involvement in pulmonary embolism (PE) has rarely been reported but is essential for critically ill and emergency patients. The aim of the present study was to analyze the diagnostic accuracy of true fast imaging with steady-state precession (true FISP), MR pulmonary angiography (MRPA) and volume-interpolated body examination (VIBE) for PE detection in comparison to CT pulmonary angiography (CTPA), which is the reference standard. A total of 21 patients with confirmed deep venous thrombosis suspected of having PE were enrolled. Emboli were evaluated on per-patient and per-vessel bases. The evidence of PE on a per-vessel basis was classified into central, lobar and segmental levels, and 27 vessel segments per patient were analyzed for a total of 567 vessel segments in all patients. The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated. Receiver operating characteristic curves were drawn to compare differences in sequences. A total of 158 pulmonary vessels were involved with emboli on CTPA, 58 of which were identified by true FISP, 63 by MRPA and 94 by VIBE. On per-patient and per-vessel bases, the sensitivity was 81.3 and 36.7%, respectively, for true FISP, 82.4 and 56.3%, respectively, for MRPA, and 94.4 and 68.1%, respectively, for VIBE; the specificity was 80.0 and 99.8%, respectively, for true FISP, 100 and 99.2%, respectively, for MRPA, and 100 and 99.2%, respectively, for VIBE. The respective PPV was 92.9 and 98.3% for true FISP, 100 and 95.5% for MRPA, 100 and 96.9% for VIBE. The NPV was 57.1 and 80.3%, respectively, for true FISP, 50.0 and 88.2%, respectively, for MRPA, and 75.0 and 89.8%, respectively, for VIBE. In conclusion, enhanced VIBE surpassed the other two sequences in revealing PE, particularly in segmental analysis, which is essential for emergency patients who have contraindications for receiving iodinated contrast and those who have concerns about the ionizing radiation.

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Abbreviations: PE, pulmonary embolism; CTPA, computed tomography pulmonary angiography; true FISP, true fast imaging with steady-state precession; MRPA, magnetic resonance pulmonary angiography; VIBE, volume-interpolated body examination; PPV, positive predictive value; NPV, negative predictive value; ROC, receiver operating characteristic; AUC, the area under the curve

Key words: MRI, pulmonary embolism, MR angiography, CT angiography, volume-interpolated body examination

Introduction

Pulmonary embolism (PE) is a fatal disease of the cardiovascular system with nonspecific clinical symptoms and significant potential morbidity and mortality (1). In the US, PE is considered to be the third leading cause of cardiovascular death after myocardial infarction and stroke (2,3). In China, the annual incidence of PE sharply increased from 0.0% in 1997 to 0.1% in 2003, and then remained at 0.1% through to 2008; the case fatality rate decreased from 25.1% in 1997 to 8.6% in 2008 in a multicenter registration study of 16,972,182 hospital admissions, among which a total 18,206 patients were confirmed to have PE (4). Patients with no definitive diagnosis had a mortality rate of 30% if untreated, 11% of patients died within the first hour of admission to hospitals (5) but the mortality rate may be <10% if patients are diagnosed and treated in time (6,7). CT pulmonary angiography (CTPA) is currently considered as the first-line modality and the reference standard for PE diagnosis due to its high diagnostic accuracy (8,9). However, avoiding X-ray radiation is of great concern for younger patients and pregnant females. Furthermore, certain patients have allergic reactions to CT iodinated contrast material. The incidence of contrast material-related nephropathy after CTPA may reach 4% overall and 12% in patients with paired (pre- and post-CTPA) creatinine measurements (10).

As an ionizing radiation-free method, MRI offers an alternative to CTPA for pulmonary vasculature evaluation (11,12) that does not require iodinated contrast material, and the combination of a comprehensive MR scanning protocol is able to achieve a performance close to that of CTPA (13,14), including various MR sequences such as true fast imaging with steady-state precession (true FISP), T2-weighted single-shot half-Fourier turbo spin echo, MR pulmonary perfusion imaging and contrast-enhanced MR pulmonary angiography (MRPA) by using a three-dimensional (3D) fast low-angle shot spoiled gradient echo (FLASH) and contrast-enhanced volumetric interpolated body examination (VIBE). However, the longer examination time and the requirements for patients to hold their breath multiple times during MR pulmonary imaging have limited the widespread application of MRI for the primary diagnosis of PE in clinical practice. For certain critically ill patients who cannot tolerate a long scanning time and numerous breath-hold sequences (15), it is necessary and important to scan the most accurate MR sequences as fast as possible in order to obtain the highest accuracy for PE diagnosis with a relatively short acquisition time.

The accuracy of MRI for PE detection has been studied based on different MR protocols in different centers and the evaluations were generally performed on per-patient, per-embolus or per-lobe bases (12,13,15,16), but the diagnostic performance of MR sequences for displaying different levels of pulmonary arteries affected by emboli has rarely been reported. Therefore, the present study aimed to investigate the diagnostic accuracy of three MR sequences that were clinically used at our hospital for PE diagnosis on per-patient and per-vessel bases, including true FISP, contrast-enhanced MRPA and VIBE compared with CTPA, in order to focus on a more relatively time-effective MR sequence, particularly for emergency patients.

Materials and methods

Study population. The present prospective study was approved by The Medical Ethics Committee of Huazhong University of Science and Technology and written informed consent was obtained from all patients. One of the patients was 17 years old and written informed consent was obtained from this patient himself and his legal guardians. A total of 21 patients [15 males, 6 females; mean age, 51.38±5.70 years (range, 17 to 66 years)] with confirmed deep venous thrombosis with suspected acute PE underwent 320-multidetector CTPA between January 2017 and December 2017, and they all agreed to undergo MRI examinations within 24 h after CTPA. Of all the patients, 3 had received recent surgical treatment, 2 had a history of malignancy, 2 had a recent history of trauma, 3 had moderate to severe arterial stenosis of the lower limbs, 2 had a history of varicose veins of the lower extremities and the remaining patients had no definite reason for leg swelling and pain. The most commonly present chest symptoms were chest pain, cough and sudden shortness of breath. The exclusion criteria were as follows: i) Pregnancy; ii) inability to undergo MRI (e.g. due to severe dyspnea, continuous cough or shock); iii) contraindications for MRI examination, including adverse reactions to MR contrast material; and iv) acute or chronic severe renal impairment (estimated glomerular filtration rate <30 ml/min/1.73 m^2).

CTPA protocol. CTPA scans were acquired on a 320-multidetector CT scanner (Aquilion One; Toshiba Medical Systems). A single bolus of 40 ml nonionic contrast agent (300 mgI/ml; Lomeron; Patheon Italia S.P.A.) was injected by a power injector (Stellant, CT injection system MedRad; Bayer Healthcare) through an intravenous antecubital catheter at 4.5 ml/sec, followed by a 40 ml saline bolus at 4.5 ml/sec. The threshold level for triggering was set at 80 HU and the region of interest (ROI) was placed in the main trunk of the pulmonary artery. Image acquisition was started 3 sec after exceeding the threshold of the measured ROI. The scanning parameters were as follows: Field of view, 35 cm; tube voltage, 100 kV; tube current, 100 mA with an automatic tube current modulation technique; gantry rotation time, 0.5 sec; collimation, 160x0.5 mm; and slice thickness, 1 mm with an 0.8-mm interval. Patients were instructed to hold their breath 2 times for 8-10 sec each time.

MRI. MRI was performed with a 1.5 T MR scanner (Magnetom Aera; Siemens Medical Systems). Patients were positioned in a supine position with the head oriented toward the magnet. One abdominal surface flex coil with 18 channels covered the chest area. Gadopentetate dimeglumine (Magnevist; Bayer Schering Pharma AG) was injected into the right antecubital vein via a 22-gauge needle using a power injector (Spectris; MedRad). The MRPA sequence was initiated by using the bolus tracking technique, with 0.1 mmol/kg contrast material injected at 2.5 ml/sec and followed by a 15-ml saline flush at 2.5 ml/sec.

MR scanning was performed in a fixed order with the following sequences: i) True FISP in coronal and axial orientations without contrast material and no need for breath-hold; ii) contrast-enhanced MRPA scanned by subtraction of 3D-FLASH sequences from prior to and after administration of the contrast agent in coronal orientation, with 3 times for breath-hold, including one time for pre-contrast and the other two times for post-contrast for 18 sec each time; and iii) T1-weighted fat-suppressed VIBE in coronal and axial orientations with 3 times for breath-hold, 18 sec each time. The detailed parameters are listed in Table I.

Data analysis. PE diagnosis on MR scans was made according to the presence of an intraluminal filling defect in the pulmonary arteries or the complete absence of vessel enhancement (16,17). The results of three sequences were initially confirmed by using CTPA as the reference standard.

CTPA images were retrospectively reviewed by two radiologists [X.K. and H.M. with 13 and 15 years of experience, respectively, in both chest CT and MRI] who were blinded to the MR images. If there was a disagreement between judgements of the two radiologists, a consensus was obtained for the final results after discussion. The location and presence of emboli on CTPA were recorded in each pulmonary artery by anatomic distribution. To determine the effect of recall bias on accuracy in the current study,

Table I. Detailed parameters of true FISP, contrast-enhanced MRPA and VIBE sequences.

Parameters	true FISP	MRPA	VIBE
Field of view (mm)	400	400	400
Repetition time (msec)	3.78	2.82	3.55
Echo time (msec)	1.89	0.94	1.35
Flip angle (degrees)	70	25	25
Slice thickness (mm)	4.0	1.4	1.5
Base resolution	256	384	448
Phase resolution (%)	100	70	75
Bandwidth (Hz/Px)	1028	450	470

True FISP, true fast imaging with steady-state precession; MRPA, magnetic resonance pulmonary angiography; VIBE, volume-interpolated body examination.

>3 months later, the two radiologists analyzed the same MR images for the evidence of pulmonary emboli, which was classified into central, lobar and segmental levels by pulmonary arterial distribution. The central level contained the main pulmonary trunk, the left pulmonary artery and the right pulmonary artery. The lobar level was divided into the right upper, middle and lower lobes; left upper lobe; lingula and left lower lobe. The segmental level contained 18 segmental pulmonary arteries. Therefore, emboli were assessed for 27 vessel segments per patient for a total of 567 vessel segments in 21 patients.

If examination of more than three lobar or half of the segmental pulmonary arteries failed to achieve diagnostic quality, the entire sequence was defined as nondiagnostic. If images of all three of the sequences were nondiagnostic, the whole MR scan for the patient was defined as a failed MR examination. A single vessel was considered nondiagnostic if the vessels were not recognizable for identification or exclusion of PE due to vascular ambiguity (18). If there were no significant respiratory motion artifacts and there was clear visualization of the segmental pulmonary arteries, the images were defined as satisfactory (19). The number and anatomical location of emboli were recorded for further calculation. The evaluation was performed and represented a consensus interpretation. The CT and MR results previously obtained were compared >2 months later to examine if emboli detected on MRI were observed as corresponding lesions on CTPA.

Statistical analysis. Data of three sequences for presence of PE was classified into 1 (PE positive) and 0 (PE negative). The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of each sequence for PE detection were calculated. Receiver operating characteristic (ROC) curve analysis was used to calculate the area under the curve (AUC) using 95% confidence intervals (CIs). The method by Delong *et al* (20) was used to compare the AUCs between different sequences by MedCalc software (version 18.11.3; MedCalc Software, Ltd). $P<0.05$ was considered to indicate a statistically significant difference.

Results

General. None of the patients failed the whole MR scans. Representative images of true FISP, MRPA and VIBE with negative PE are presented in Fig. 1. Only one patient exhibited a mild allergic reaction after CTPA scanning (Fig. 2), while all other patients completed MR scanning successfully without any allergic reactions. CTPA revealed 45 pulmonary emboli in total, while MRI detected 36 in total, including 23 with true FISP, 25 with MRPA and 36 with VIBE. Of the 9 emboli not identified by MRI, 7 were in the segmental pulmonary arterial branches and the other 2 were in the truncation between lobar and segmental levels.

Analysis on a per-patient basis. CTPA revealed PE in 18 patients, while MRI detected PE in 17 patients. The one patient missed by MRI had only one small isolated embolus in a segmental pulmonary arterial branch. True FISP indicated one false-positive finding due to misinterpretation of the pulmonary vein as a pulmonary artery. MRPA of one patient was excluded from the final results due to severe respiratory motion artifacts caused by coughing during the acquisition. The differences for PE detection were not significant (true FISP vs. MRPA: $P=0.2466$; true FISP vs. VIBE: $P=0.1414$; MRPA vs. VIBE: $P=0.1441$; Table II). The ROC curves are displayed in supplementary material of Fig. S1A.

Analysis on a per-vessel basis. A total of 158 pulmonary vessels (27.9%, 158/567) were affected by emboli on CTPA and 97 of them (17.1%, 97/567) were identified on MRI. Altogether, 29 vessels (5.1%, 29/567) were excluded from comparison between CTPA and MRI, as those vessels were excluded simultaneously in two MR sequences. A total of 58 vessels (10.2%, 58/567) with emboli involvement were detected by true FISP, 62 by MRPA (10.9%, 62/567) and 94 by VIBE (16.6%, 94/567). By contrast, 87 vessels from MRPA (15.3%, 87/567) and 37 from VIBE (6.5%, 37/567) were excluded from the evaluation due to severe respiratory motion artifacts, pleural effusion and pulmonary atelectasis.

The differences in the AUCs among the three sequences based on pulmonary arterial vessels were significant (true FISP vs. MRPA: $P=0.0016$; true FISP vs. VIBE: $P<0.0001$; MRPA vs. VIBE: $P=0.0004$; Table II). The ROC curves are displayed in Fig. S1B. On per-patient and per-vessel bases, true FISP had an accuracy of 81.0 and 82.2% respectively, MRPA had an accuracy of 85.0 and 89.2% respectively, and VIBE had an accuracy of 95.2 and 91.1% respectively; the sensitivity for true FISP was 81.3 and 36.7% respectively, for MRPA was 82.4 and 56.3% respectively, and for VIBE was 94.4 and 68.1% respectively; the specificity for true FISP was 80.0 and 99.8% respectively, for MRPA was 100 and 99.2% respectively, and for VIBE was 100 and 99.2% respectively. The respective PPV was 92.9 and 98.3% for true FISP, 100 and 95.5% for MRPA, 100 and 96.9% for VIBE. The NPV was 57.1 and 80.3% respectively for true FISP, 50.0 and 88.2% respectively for MRPA, and 75.0 and 89.8% respectively for VIBE.

All the central pulmonary arteries were classified as assessable for PE detection. CTPA revealed 10 central pulmonary arteries with emboli; 9 were detected by true FISP, 8 by MRPA and 10 by VIBE. The differences in the AUCs among

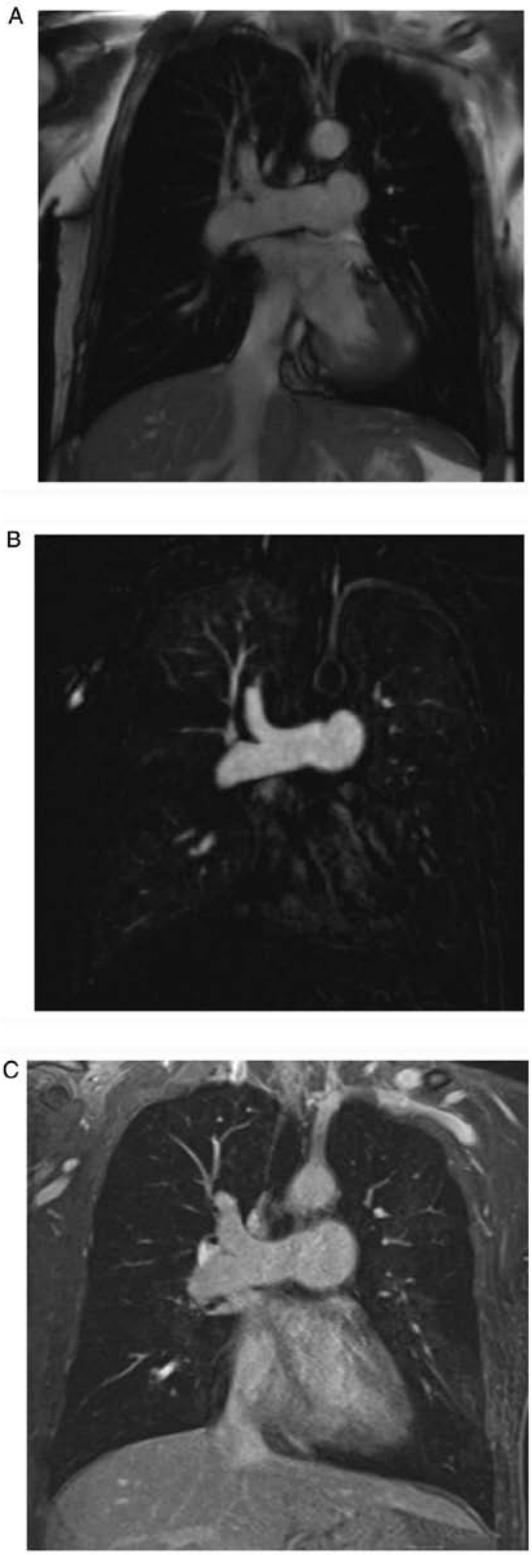

Figure 1. Representative coronal images of a 57-year-old male with deep venous thrombosis acquired without involvement of pulmonary embolism. (A) True fast imaging with steady-state precession, (B) magnetic resonance pulmonary angiography and (C) volume-interpolated body examination.

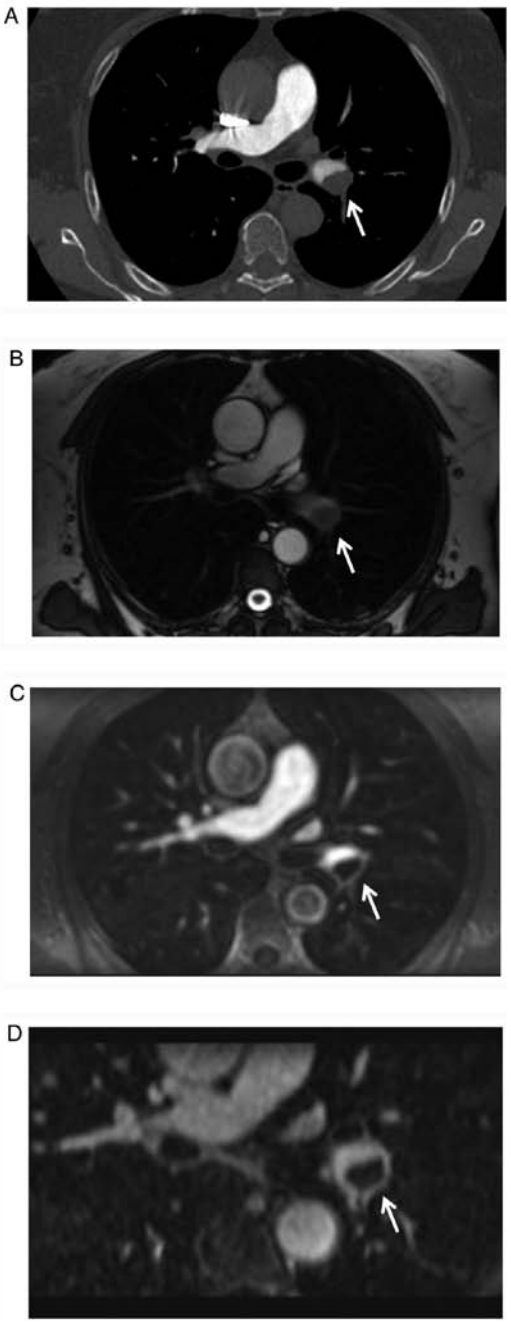

Figure 2. Pulmonary embolus in the left lower lobe in a 65-year-old male who presented with leg swelling for five days. After CTPA scanning, this patient displayed mild allergic reactions to the iodine contrast material, with symptoms including nausea, sweating and itchy skin, but he displayed with no allergic reactions to MR gadolinium-based contrast material. The embolus was visualized by (A) CTPA, (B) true fast imaging with steady-state precession, (C) contrast-enhanced MR pulmonary angiography and (D) enhanced volume-interpolated body examination, all of which depicted the lesion clearly (arrows) in the axial images. CTPA, computed tomography pulmonary angiography.

the three sequences based on the pulmonary arterial segments were not significant (true FISP vs. MRPA: P=0.3173; true FISP vs. VIBE: P=0.3173; MRPA vs. VIBE: P=0.1336; Table III). The ROC curves are displayed in supplementary material of Fig. S2A.

For the analysis at the pulmonary lobar level, 22 pulmonary arterial vessels from MRPA and 8 from VIBE were excluded from the assessment due to severe respiratory motion artifacts. CTPA revealed 40 lobar pulmonary arteries with emboli, while true FISP detected 29; MRPA 24 and VIBE detected 31. The differences in the AUCs among the three sequences based on the pulmonary lobes were not significant (true FISP

Table II. Diagnostic performance and statistical results of MR sequences for pulmonary emboli detection on a per-patient basis (A) and per-vessel basis (B).

A, Per-patient basis

	Number of patients				MR diagnostic performance				ROC curve analysis results	
MR sequence	TP	FP	FN	TN	Sens. (%)	Spec. (%)	PPV (%)	NPV (%)	AUC	95% CI
True FISP	13	1	3	4	81.3	80.0	92.9	57.1	0.716	0.473-0.892
MRPA	14	0	3	3	82.4	100.0	100.0	50.0	0.912	0.698-0.991
VIBE	17	0	1	3	94.4	100.0	100.0	75.0	0.971	0.782-1.000

B, Per-vessel basis

	Number of patients				MR diagnostic performance				ROC curve analysis results	
MR sequence	TP	FP	FN	TN	Sens. (%)	Spec. (%)	PPV (%)	NPV (%)	AUC	95% CI
True FISP	58	1	100	408	36.7	99.8	98.3	80.3	0.692	0.647-0.734
MRPA	63	3	49	365	56.3	99.2	95.5	88.2	0.785	0.744-0.822
VIBE	94	3	44	389	68.1	99.2	96.9	89.8	0.873	0.839-0.902

True FISP, true fast imaging with steady-state precession; MRPA, magnetic resonance pulmonary angiography; VIBE, volume-interpolated body examination; TP, true-positive results; TN, true-negative results; FP, false-positive results; FN, false-negative results; Sens., sensitivity; Spec., specificity; PPV, positive predictive value; NPV, negative predictive value; AUC, area under the curve; ROC, receiver operating characteristic.

vs. MRPA: P=0.3173; true FISP vs. VIBE: P=0.1179; MRPA vs. VIBE: P=0.4375; Fig. 2; Table III). The ROC curves are displayed in Fig. S2B.

Regarding the evaluation of the segmental pulmonary vessels, 65 from MRPA and 29 from VIBE were excluded from evaluation due to severe respiratory motion artifacts, pleural effusion and pulmonary atelectasis. CTPA revealed 108 segmental pulmonary arteries affected by emboli, while true FISP detected 20, MRPA 30 and VIBE detected 53. The differences in the AUCs among the three sequences were significant (true FISP vs. MRPA: P=0.0008; true FISP vs. VIBE: P<0.0001; MRPA vs. VIBE: P=0.0014; Figs. 3 and 4; Table III). The ROC curves were displayed in supplementary material of Fig. S2C. From central-lobar level to the segmental level, sensitivity of true FISP changed from 70.7-90.0 to 18.5%, specificity ranged from 99.6-100%; sensitivity of MRPA changed from 70.6-80.0 to 41.7%, specificity ranged from 98.6-100%; sensitivity of VIBE changed from 86.1-100 to 73.6%, specificity ranged from 98.8-100%.

Discussion

The present study aimed to investigate the diagnostic value of three MR sequences (true FISP, MRPA and VIBE) for PE detection compared with CTPA. The results revealed enhanced VIBE to be the most accurate sequence, with 95.2% accuracy on a per-patient basis and 91.1% accuracy on a per-vessel basis.

The three sequences evaluated in the present study were most commonly used in everyday clinical practice at our hospital and patients were only required to hold their breath 6 times during the whole protocol. The total time for patients on the scanner bed was controlled within 10 min, which achieved a relatively fast MR protocol for patients suspected of having PE. Indeed, radiologists were not able to diagnose PE on MRI by evaluating only one sequence in clinical practice, but it is necessary to determine the diagnostic ability of different sequences for PE, particularly for emergency patients and critically ill patients. For those patients, particularly when they have contraindications for CTPA, contrast-enhanced VIBE should be preferentially considered.

True FISP in MRI has been proven to be useful for depicting lung parenchyma and the pulmonary vasculature without the requirement for breath-holding or contrast material (18). Since it is a true fast imaging technique with steady-state precession sequences that can generate predominantly T2-weighted contrast images, true FISP is able to depict the vessel wall and embolus clearly as the thrombi displays hypointensity. Furthermore, this sequence is not sensitive to motion degradation, allowing patients who cannot successfully hold their breath to be scanned. It has been reported to achieve 62-93% sensitivity and 95-100% specificity (13,15,16,21). Similar to those results, the present study determined that true FISP had a specificity of 80.0 and 99.8% on a per-patient basis and per-vessel basis, respectively, and the sensitivity was 81.3% in the per-patient analysis but only 36.7% in the per-vessel analysis. For different levels of the pulmonary arteries, the specificity ranged from 99.6 to 100% irrespective of the location of pulmonary vessels, while the sensitivity decreased

Table III. Diagnostic accuracy of MR sequences for detecting pulmonary embolism at the central, lobar and segmental pulmonary levels.

A, Central pulmonary arterial level

	Number of vessels				MR diagnostic performance				ROC curve analysis results	
MR sequences	TP	FP	FN	TN	Sens. (%)	Spec. (%)	PPV (%)	NPV (%)	AUC	95% CI
True FISP	9	0	1	53	90.0	100.0	100.0	98.1	0.950	0.864-0.989
MRPA	8	0	2	53	80.0	100.0	100.0	96.4	0.900	0.798-0.961
VIBE	10	0	0	53	100.0	100.0	100.0	100.0	1.000[a]	0.943-1.000

B, Lobar level

MR sequences	TP	FP	FN	TN	Sens. (%)	Spec. (%)	PPV (%)	NPV (%)	AUC	95% CI
True FISP	29	0	12	85	70.7	100.0	100.0	87.6	0.862	0.778-0.923
MRPA	24	1	10	69	70.6	98.6	96.0	87.3	0.914	0.840-0.961
VIBE	31	1	5	81	86.1	98.8	96.9	94.2	0.941	0.875-0.978

C, Segmental level

MR sequences	TP	FP	FN	TN	Sens. (%)	Spec. (%)	PPV (%)	NPV (%)	AUC	95% CI
True FISP	20	1	88	269	18.5	99.6	95.2	75.4	0.580	0.521-0.637
MRPA	30	2	42	239	41.7	99.2	93.8	85.1	0.712	0.657-0.763
VIBE	53	2	39	255	73.6	99.2	96.4	86.7	0.824	0.776-0.866

[a]AUC=1.00 may be due to the limited sample size (n=63) for central vessel analysis. True FISP, true fast imaging with steady-state precession; MRPA, magnetic resonance pulmonary angiography; VIBE, volume-interpolated body examination; TP, true-positive results; TN, true-negative results; FP, false-positive results; FN, false-negative results; Sens., sensitivity; Spec., specificity; PPV, positive predictive value; NPV, negative predictive value; AUC, area under the curve; ROC, receiver operating characteristic.

from the central-lobar level (70.7-90.0%) to the segmental level (18.5%) and its ability to depict the peripheral pulmonary vasculature was diminished more than that for the central pulmonary arteries (22), which is in accordance with previous studies (13,23); however, the sensitivity at the segmental level (18.5%) was lower than that determined in previous studies (41.7 and 62.0%). This discrepancy may be due to the different analyses, as a per-vessel analysis was employed to detect the vessels that were involved with emboli at different levels; this discrepancy may also be attributed to different thrombus distributions in different studies. The present results initially validated true FISP to be feasible for PE detection in the central and lobar pulmonary arteries, but inadequate for the segmental emboli with only 18.5% sensitivity.

It has been reported that the incidence of severe acute adverse reactions associated with gadolinium-based contrast material is lower than that of iodinated contrast agents (24,25), and a large number of clinical studies related to MR for PE diagnosis have been performed using contrast-enhanced MR (12,13,16,23). As contrast-enhanced MRPA is a fast and flow-independent method for assessing pulmonary vasculature, it is able to avoid saturation effects and offer a substantially higher resolution than non-contrast techniques. On per-patient and per-vessel bases, MRPA in the present study had an accuracy of 85.0 and 89.2%, respectively, a sensitivity of 82.4 and 56.3%, respectively, and a specificity of 100 and 99.2%, respectively. For different levels of the pulmonary arteries, the sensitivity of MRPA decreased from the central-lobar level (70.6-80.0%) to the segmental level (41.7%), but the specificity ranged from 98.6 to 100%, irrespective of the different levels of the pulmonary vessels. These results were consistent with the largest report that focused on the accuracy of contrast-enhanced MRPA for acute PE diagnosis (12), in which technically adequate MRPA had a 78% sensitivity and 99% specificity; the sensitivity for PE at the main or lobar level was 79% and the specificity was 98-100% irrespective of the order of the pulmonary vessels. The sensitivity of MRPA on a per-lobe basis in the present study was similar to that determined by Zhang *et al* (26), in which lobar, segmental and subsegmental emboli were assigned to the distribution of the lobar pulmonary artery-supplying territory. By contrast, in the present study, the diagnostic performance was evaluated based on different pulmonary arterial levels; thus, sensitivity on a per-vessel basis (56.3%) and on a per-segmental basis (41.7%) was lower than those determined by the above study.

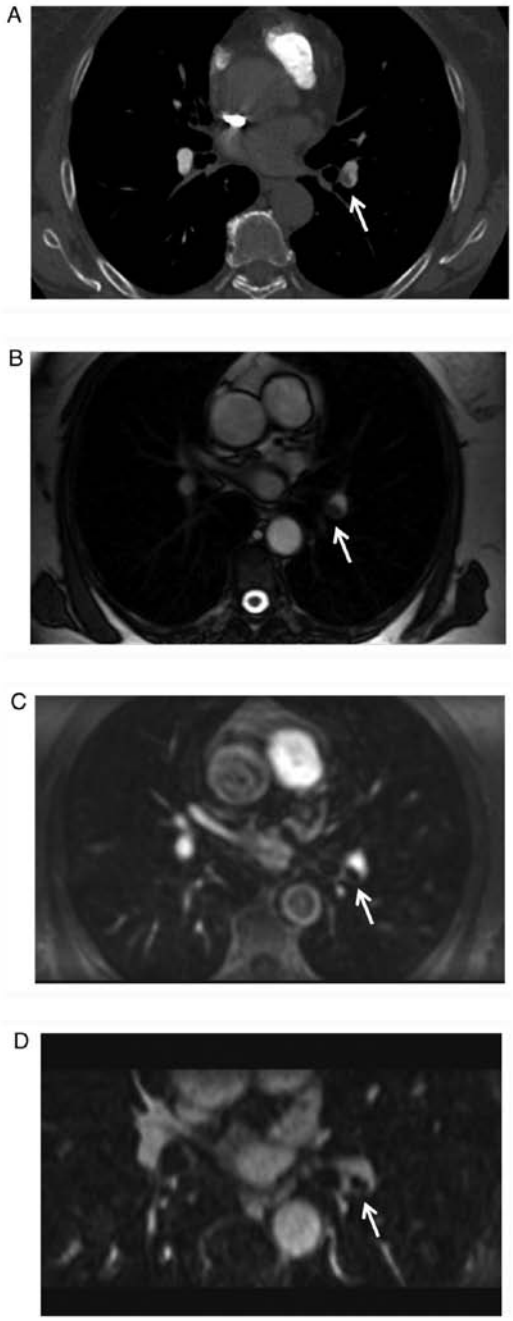

Figure 3. Representative case of a 63-year-old male with leg pain and chest congestion. (A) CT pulmonary angiography revealed the pulmonary embolus at the truncation of the segmental pulmonary artery in the left lower lobe (arrow). (B-D) Axial images of (B) true fast imaging with steady-state precession, (C) contrast-enhanced MR pulmonary angiography and (D) enhanced volume-interpolated body examination displayed the embolus depicted in A clearly (arrows).

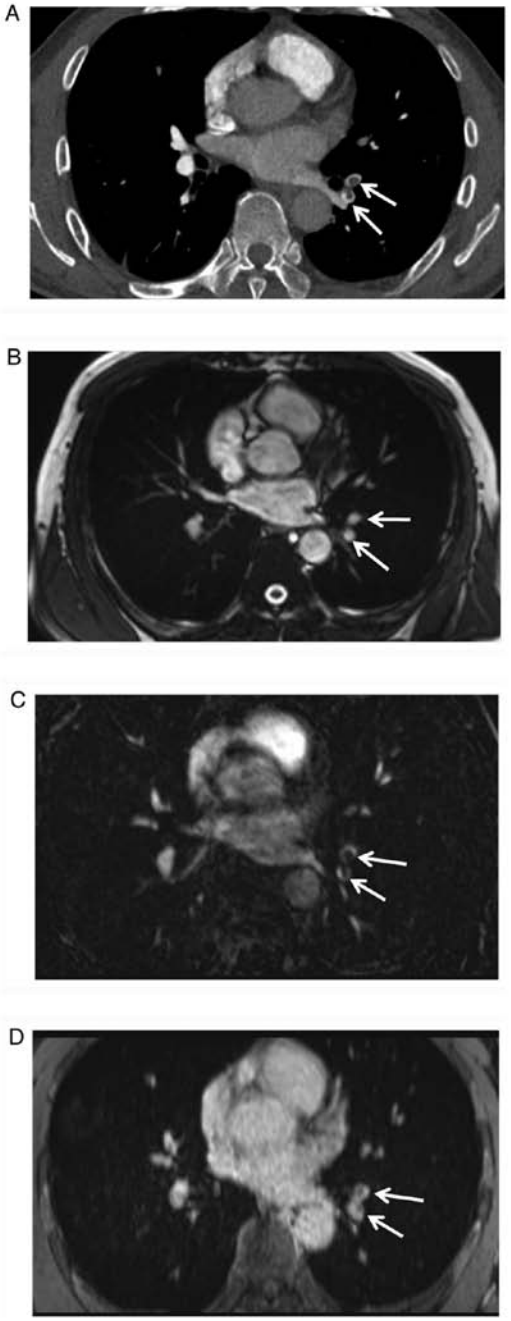

Figure 4. Representative case of a 49-year-old female with segmental pulmonary embolism. (A) CT pulmonary angiography revealed emboli in the lateral and posterior basal segmental pulmonary arteries (arrows). (B) True fast imaging with steady-state precession axial image failed to depict the emboli displayed in A. (C) Contrast-enhanced MR pulmonary angiography and (D) enhanced volume-interpolated body examination successfully displayed the emboli depicted in A clearly in the axial images.

By analyzing emboli that were not depicted by MRPA at the central and lobar levels, it was determined that those emboli were located at the truncation of central and lobar pulmonary vessels and adhered to the vessel wall instead of localizing at the center of the vessel lumen. The subtraction of MRPA provides visualization of the vessel lumen with the help of contrast material, but it has a limited ability to display the vessel wall, which makes it difficult to visualize an eccentric thrombus, particularly when the emboli are adherent to the vessel wall (16).

Enhanced VIBE has been widely used for delineating vasculatures such as the pulmonary arteries (27) and the venous system of the lower legs (23,27-29), as this sequence enables the vessel wall to be visualized and the intraluminal emboli to be outlined with the help of contrast material. With a high resolution and low slice thickness, on a per-patient basis and per-vessel basis in the present study, this sequence had an accuracy of 95.2 and 91.1%, respectively, a sensitivity of 94.4 and 68.1%, respectively, and a specificity of 100 and 99.2% respectively; the highest AUC in the ROC curve evaluation was obtained

at the central, lobar and segmental levels, and a significant difference was detected, particularly at the segmental level, which proved VIBE to be the most accurate sequence for PE detection among the three sequences. This result is consistent with that of Kalb *et al* (16), who evaluated the presence of PE based on eight pulmonary arteries and/or vascular territories, and segmental and subsegmental emboli were assigned to the vascular distribution of the lobar pulmonary arteries. However, in contrast with their investigation, the present study included patients with identified deep venous thrombosis who were suspected to have acute PE, and an evaluation was performed based on the central, lobar, segmental pulmonary arteries to investigate the abilities of three sequences to depict the vessels affected by emboli. Due to the recirculation phases of contrast enhancement in VIBE sequence, it demands less experience for MR operators as it is able to eliminate the timing failures in capturing the peak enhancement of the pulmonary arteries, which may be a limitation of contrast-enhanced MRPA.

CTPA has been applied in routine work, even for severe cases and dyspneic patients in emergency settings, and only requires short, infrequent breath-holds (30); however, for patients who are allergic to iodinated contrast material and particularly young patients who are aware of the ionizing radiation involved within CTPA, MRI serves as an alternative method for pulmonary imaging, as it requires neither ionizing radiation nor the use of iodinated contrast material. However, it is still challenging in severely ill patients because of the longer scan times and multiple breath-holds required in different MR protocols. A reduced duration and frequency of breath-holds is associated with better patient cooperation. Of note, shorter breath-holds resulted in decreased motion artifacts; therefore, it is crucial to keep the breath-hold time as short as possible. In the present study, even though patients were only required to hold their breath 6 times for 18 sec each time, the fact that certain pulmonary vessels with severe motion artifacts failed to receive a clear diagnosis was still a major drawback for MRI. Therefore, it is necessary to determine the sequence with the most accurate results. When patients have difficulty in completely cooperating for the whole MR scanning protocol, contrast-enhanced VIBE is adequate only with 2-3 times of breath-hold for axial and coronal PE imaging (31). However, among the excluded vessels in the per-vessel analysis, including 15.3% (87/567) of the pulmonary arteries from MRPA, 6.5% (37/567) of those from VIBE and an overall 5.1% (29/567) of the pulmonary arteries from the combined MR protocol, 38.6% (61/158) of the vessels affected by emboli were still missed by MRI; these results also supported the lower diagnostic performance of MRI as compared with that of CTPA for PE diagnosis.

The present study had several limitations: First, the number of enrolled patients was relatively small. Furthermore, evaluation of subsegmental pulmonary arteries was not performed, because the sensitivity of MRI for subsegmental emboli remains insufficient (12,16,21,30). In addition, in a previous study (9), which focused on the comparison of diagnostic accuracy for acute PE between CTPA and pulmonary angiography, subsegmental PE were detected in 15 patients in pulmonary angiography, whilst CTPA failed to demonstrate the subsegmental vessel involvement in 8 of the 15 patients tested (53%). Certain other advanced MR techniques, such as time-resolved contrast-enhanced MR angiography, radial VIBE, dynamic contrast-enhanced MR perfusion and quiescent-interval single-shot techniques (32) should also be considered in future studies. As another limitation, the higher cost of MRI in comparison with that of CTPA has limited its wide-spread application in practice. Finally, bias may exist due to the fixed order and different slice thicknesses of the three sequences in the present study.

In conclusion, enhanced VIBE surpassed the other two sequences in revealing PE, with 95.2% accuracy for the per-patient analysis and 91.1% accuracy for the per-vessel analysis, particularly for segmental pulmonary PE, which is essential for emergency patients who have contraindications to iodinated contrast and those who have great concerns about ionizing radiation.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

QF: Conceptualization, writing, project administration, review and editing; QC: Methodology, review and editing; XK and HM: Visualization, formal analysis; ZL: Methodology, formal analysis. All authors contributed to the study conception and design. All authors read and approved the final manuscript.

Ethics approval and consent to participate

This prospective study was approved by the Medical Ethics Committee of Tongji Medical College, Huazhong University of Science and Technology (Wuhan, China). Patients were informed of the procedures and the purpose of this study, and written consent was obtained.

Patient consent for publication

All the patients provided written informed consent for the publication of the associated data and accompanying images.

Competing interests

The authors declare that they have no competing interests.

References

1. Uresandi F, Monreal M, García-Bragado F, Domenech P, Lecumberri R, Escribano P, Zamorano JL, Jimenez S, Ruiz-Artacho P, Lozano F, *et al*: National consensus on the diagnosis, risk stratification and treatment of patients with pulmonary embolism. Spanish society of pneumology and thoracic surgery (SEPAR). Society Española Internal Medicine (SEMI). Spanish Society of Thrombosis and Haemostasis (SETH). Spanish Society of Cardiology (ESC). Spanish Society of Medicine Accident and Emergency (SEMES). Spanish Society of Angiology and Surgery Vascular (SEACV). Arch Bronconeumol 49: 534-547, 2013.

2. Dronkers CE, Klok FA and Huisman MV: Current and future perspectives in imaging of venous thromboembolism. J Thromb Haemost 14: 1696-1710, 2016.
3. Goldhaber SZ and Bounameaux H: Pulmonary embolism and deep vein thrombosis. Lancet 379: 1835-1846, 2012.
4. Yang Y, Liang L, Zhai Z, He H, Xie W, Peng X and Wang C; Investigators for National Cooperative Project for Prevention and Treatment of PTE-DVT: Pulmonary embolism incidence and fatality trends in Chinese hospitals from 1997 to 2008: A multicenter registration study. PLoS One 6: e26861, 2011.
5. Dalen JE: Pulmonary embolism: What have we learned since Virchow? Natural history, pathophysiology, and diagnosis. Chest 122: 1440-1456, 2002.
6. Kuriakose J and Patel S: Acute pulmonary embolism. Radiol Clin North Am 48: 31-50, 2010.
7. Nikolaou K, Thieme S, Sommer W, Johnson T and Reiser MF: Diagnosing pulmonary embolism: New computed tomography applications. J Thorac Imaging 25: 151-160, 2010.
8. Stein PD, Fowler SE, Goodman LR, Gottschalk A, Hales CA, Hull RD, Leeper KJ, Popovich JJ, Quinn DA, Sos TA, *et al*: Multidetector computed tomography for acute pulmonary embolism. N Engl J Med 354: 2317-2327, 2006.
9. Winer-Muram HT, Rydberg J, Johnson MS, Tarver RD, Williams MD, Shah H, Namyslowski J, Conces D, Jennings SG, Ying J, *et al*: Suspected acute pulmonary embolism: Evaluation with multi-detector row CT versus digital subtraction pulmonary arteriography. Radiology 233: 806-815, 2004.
10. Mitchell AM and Kline JA: Contrast nephropathy following computed tomography angiography of the chest for pulmonary embolism in the emergency department. J Thromb Haemost 5: 50-54, 2007.
11. Mudge CS, Healey TT, Atalay MK and Pezzullo JA: Feasibility of detecting pulmonary embolism using noncontrast MRI. ISRN Radiol 2013: 729271, 2013.
12. Stein PD, Chenevert TL, Fowler SE, Goodman LR, Gottschalk A, Hales CA, Hull RD, Jablonski KA, Leeper KV Jr, Naidich DP, *et al*: Gadolinium-enhanced magnetic resonance angiography for pulmonary embolism: A multicenter prospective study (PIOPED III). Ann Intern Med 152: 434-443, 2010.
13. Hosch W, Schlieter M, Ley S, Heye T, Kauczor HU and Libicher M: Detection of acute pulmonary embolism: Feasibility of diagnostic accuracy of MRI using a stepwise protocol. Emerg Radiol 21: 151-158, 2014.
14. Revel MP, Sanchez O, Lefort C, Meyer G, Couchon S, Hernigou A, Niarra R, Chatellier G and Frija G: Diagnostic accuracy of unenhanced, Contrast-enhanced perfusion and angiographic MRI sequences for pulmonary embolism diagnosis: Results of independent sequence readings. Eur Radiol 23: 2374-2382, 2013.
15. Pasin L, Zanon M, Moreira J, Moreira AL, Watte G, Marchiori E and Hochhegger B: Magnetic resonance imaging of pulmonary embolism: Diagnostic accuracy of unenhanced MR and influence in mortality rates. Lung 195: 193-199, 2017.
16. Kalb B, Sharma P, Tigges S, Ray GL, Kitajima HD, Costello JR, Chen Z and Martin DR: MR imaging of pulmonary embolism: Diagnostic accuracy of contrast-enhanced 3D MR pulmonary angiography, contrast-enhanced low-flip angle 3D GRE, and nonenhanced Free-induction FISP sequences. Radiology 263: 271-278, 2012.
17. Mamlouk MD, VanSonnenberg E, Gosalia R, Drachman D, Gridley D, Zamora JG, Casola G and Ornstein S: Pulmonary embolism at CT angiography: Implications for appropriateness, cost, and radiation exposure in 2003 patients. Radiology 256: 625-632, 2010.
18. Kluge A, Muller C, Hansel J, Gerriets T and Bachmann G: Real-time MR with TrueFISP for the detection of acute pulmonary embolism: Initial clinical experience. Eur Radiol 14: 709-718, 2004.
19. Schiebler ML, Nagle SK, Francois CJ, Repplinger MD, Hamedani AG, Vigen KK, Yarlagadda R, Grist TM and Reeder SB: Effectiveness of MR angiography for the primary diagnosis of acute pulmonary embolism: Clinical outcomes at 3 months and 1 year. J Magn Reson Imaging 38: 914-925, 2013.
20. DeLong ER, DeLong DM and Clarke-Pearson DL: Comparing the areas under two or more correlated receiver operating characteristic curves: A nonparametric approach. Biometrics 44: 837-845, 1988.
21. Kluge A, Mueller C, Strunk J, Lange U and Bachmann G: Experience in 207 combined MRI examinations for acute pulmonary embolism and deep vein thrombosis. AJR Am J Roentgenol 186: 1686-1696, 2006.
22. Ohno Y, Yoshikawa T, Kishida Y, Seki S and Karabulut N: Unenhanced and Contrast-enhanced MR angiography and perfusion imaging for suspected pulmonary thromboembolism. AJR Am J Roentgenol 208: 517-530, 2017.
23. Kaya F, Ufuk F and Karabulut N: Diagnostic performance of contrast-enhanced and unenhanced combined pulmonary artery MRI and magnetic resonance venography techniques in the diagnosis of venous thromboembolism. Br J Radiol 92: 20180695, 2019.
24. Prince MR, Zhang H, Zou Z, Staron RB and Brill PW: Incidence of immediate gadolinium contrast media reactions. AJR Am J Roentgenol 196: W138-W143, 2011.
25. Dillman JR, Ellis JH, Cohan RH, Strouse PJ and Jan SC: Frequency and severity of acute Allergic-like reactions to Gadolinium-containing i.v. Contrast media in children and adults. AJR Am J Roentgenol 189: 1533-1538, 2007.
26. Zhang LJ, Luo S, Yeh BM, Zhou CS, Tang CX, Zhao Y, Li L, Zheng L, Huang W and Lu GM: Diagnostic accuracy of Three-dimensional Contrast-enhanced MR angiography at 3-T for acute pulmonary embolism detection: Comparison with multidetector CT angiography. Int J Cardiol 168: 4775-4783, 2013.
27. Hansch A, Betge S, Poehlmann G, Neumann S, Baltzer P, Pfeil A, Waginger M, Boettcher J, Kaiser WA, Wolf G, *et al*: Combined magnetic resonance imaging of deep venous thrombosis and pulmonary arteries after a single injection of a blood pool contrast agent. Eur Radiol 21: 318-325, 2011.
28. Pfeil A, Betge S, Poehlmann G, Boettcher J, Drescher R, Malich A, Wolf G, Mentzel HJ and Hansch A: Magnetic resonance VIBE venography using the blood pool contrast agent gadofosveset Trisodium-an interrater reliability study. Eur J Radiol 81: 547-552, 2012.
29. Fu Q, Cheng Q, Wu S and Kong X: Fat-suppressed magnetic resonance volume interpolated examination for deep venous thrombosis compared with duplex sonography. Exp Ther Med 19: 2632-2640, 2020.
30. Squizzato A, Pomero F, Allione A, Priotto R, Riva N, Huisman MV, Klok FA, Stein PD, Guasti L, Fenoglio L, *et al*: Diagnostic accuracy of magnetic resonance imaging in patients with suspected pulmonary embolism: A bivariate Meta-analysis. Thromb Res 154: 64-72, 2017.
31. Fu Q, Liu D, Kong X and Lei Z: Combined MR imaging for pulmonary embolism and deep venous thrombosis by Contrast-enhanced MR volume interpolated body examination. Curr Med Sci 40: 192-198, 2020.
32. Edelman RR, Silvers RI, Thakrar KH, Metzl MD, Nazari J, Giri S and Koktzoglou I: Nonenhanced MR angiography of the pulmonary arteries using single-shot radial quiescent-interval slice-selective (QISS): A technical feasibility study. J Cardiovasc Magn Reson 19: 48, 2017.