JACC: CARDIOVASCULAR IMAGING VOL. 9, NO. 7, 2016

ISSN 1936-878X/$36.00
PUBLISHED BY ELSEVIER
http://dx.doi.org/10.1016/j.jcmg.2015.11.029

Detection of LA and LAA Thrombus by CMR in Patients Referred for Pulmonary Vein Isolation

Danai Kitkungvan, MD, Faisal Nabi, MD, Mohamad G. Ghosn, PhD, Amish S. Dave, MD, Miguel Quinones, MD, William A. Zoghbi, MD, Miguel Valderrabano, MD, Dipan J. Shah, MD

ABSTRACT

OBJECTIVES The goal of this study was to evaluate the diagnostic performance of a comprehensive, multicomponent cardiac magnetic resonance (CMR) study for assessment of left atrial (LA) and left atrial appendage (LAA) thrombus.

BACKGROUND Pre-operative evaluation for pulmonary vein isolation (PVI) typically requires tomographic imaging to define pulmonary venous anatomy and transesophageal echocardiogram (TEE) to assess for the presence of LA/LAA thrombus. CMR is increasingly being used to define pulmonary venous anatomy before PVI. Limited data are available on the utility of a multicomponent CMR protocol in assessing LA/LAA thrombus.

METHODS We studied patients who underwent multicomponent CMR for evaluation of pulmonary venous anatomy before PVI and underwent TEE within 7 days. LA and LAA thrombi were evaluated by using CMR as follows: 1) cine-CMR; 2) contrast-enhanced magnetic resonance angiography; and 3) equilibrium phase delayed enhancement (DE) CMR with a long inversion time (TI) of 600 ms (long TI DE-CMR). Components of the CMR study were evaluated for diagnostic performance for detection of LA or LAA thrombus using TEE as the reference standard.

RESULTS During the study period, 261 patients were assessed. The median CHA_2DS_2VASc (congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, stroke/transient ischemic attack, vascular disease, age 65 to 74 years, sex category) score was 2, and 73.6% of patients were undergoing anticoagulation therapy. CMR and TEE were performed within 1.3 ± 2.3 days. LA/LAA thrombi were discovered in 9 patients (3.5%) by using TEE. Among the CMR techniques performed, long TI DE-CMR had the highest diagnostic accuracy (99.2%), sensitivity (100%), and specificity (99.2%), followed by contrast-enhanced magnetic resonance angiography (accuracy 94.3%; sensitivity 66.7%; and specificity 95.2%) and cine-CMR (accuracy 91.6%; sensitivity 66.7%; and specificity 92.5%).

CONCLUSIONS In patients referred for PVI, CMR could be a single complete diagnostic study for assessment of pulmonary venous anatomy as well as presence of LA/LAA thrombi, thus reducing the number of pre-operative tests before PVI. Long TI DE-CMR has the best diagnostic performance and should be used for the detection of LA/LAA thrombi.
(J Am Coll Cardiol Img 2016;9:809–18) © 2016 by the American College of Cardiology Foundation.

Atrial fibrillation (AF) is one of the most commonly encountered cardiac arrhythmias in the United States as well as worldwide (1). Approximately 1% of patients with AF are <60 years of age, and up to 12% of patients with AF are >75 years of age (1). With an aging population, it is estimated that globally, 33.5 million individuals live with AF (2). The morbidity and mortality associated with AF are mainly derived from consequences of cardioembolic phenomenon. Patients with AF have a 5-fold higher risk of embolic stoke than those with sinus rhythm (2). Stagnation of blood flow in the left atrium (particularly in the blind pouch of the left atrial appendage [LAA]) and impairment of

From the Department of Cardiology, Houston Methodist DeBakey Heart & Vascular Center, Houston, Texas. The authors have reported that they have no relationships relevant to the contents of this paper to disclose. Raymond Kim, MD, served as Guest Editor for this paper.

Manuscript received June 29, 2015; revised manuscript received November 20, 2015, accepted November 24, 2015.

ABBREVIATIONS AND ACRONYMS

AF = atrial fibrillation

CI = confidence interval

CMR = cardiac magnetic resonance

CT = computed tomography

DE = delayed enhancement

LA = left atrial

LAA = left atrial appendage

MRA = magnetic resonance angiography

PVI = pulmonary vein isolation

TEE = transesophageal echocardiography

TI = inversion time

atrial contractile function are the major underlying pathophysiology of thromboembolism in patients with AF (3).

Pulmonary vein isolation (PVI) has evolved as an effective therapeutic option for patients with AF (1,4). As a part of the pre-operative preparation, cardiac computed tomography (CT) or cardiac magnetic resonance (CMR) imaging is usually performed to provide a precise map of the pulmonary venous anatomy (4). In addition, transesophageal echocardiography (TEE) is frequently performed before PVI to exclude the presence of left atrial (LA) or LAA thrombus (4). TEE is currently considered the gold standard for LA/LAA thrombus detection given its favorable sensitivity and specificity (1,4–6). With recent advances, cardiac CT scanning is now becoming another reliable diagnostic method for evaluation of thrombus in the left atrium and LAA, particularly when delayed imaging is performed (6). However, it exposes patients to increased radiation doses and a potential risk of contrast-induced nephropathy (6,7).

SEE PAGE 819

CMR is a useful imaging technique that can provide valuable information in multiple clinical scenarios such as assessment of myocardial viability, valvular function, and evaluation of the vascular system (via magnetic resonance angiography [MRA] or venography) (8). Effectiveness of left ventricular thrombus detection by CMR has been validated, and it is now becoming a preferred imaging modality for evaluation of left ventricular thrombus (8–10). To our knowledge, there are few data regarding the utility of CMR for detection of LA/LAA thrombus (11–13). The goal of the present study was to systematically evaluate the diagnostic performance of a comprehensive multicomponent CMR assessment for detection of LA/LAA thrombus in patients referred for PVI.

METHODS

PATIENT SELECTION. From January 2009 to December 2014, all patients who were referred to the Houston Methodist DeBakey Heart & Vascular Center CMR Laboratory (Houston, Texas) for pulmonary venous anatomy mapping by CMR with intravenous gadolinium were enrolled into a registry. A comprehensive medical history was obtained to calculate CHA_2DS_2VASc (congestive heart failure, hypertension, ≥75 years of age, diabetes mellitus, stroke/transient ischemic attack, vascular disease, 65 to 74 years of age, sex category) score. Only patients who underwent TEE for assessment of LA/LAA thrombus within 7 days of the CMR procedure were included in this analysis. The study was approved by the institutional review board of the Houston Methodist Research Institute, and written informed consent was obtained from all subjects.

CMR PROTOCOLS. CMR was performed with either 1.5- or 3-T whole-body clinical scanners (Siemens Avanto and Siemens Verio; Siemens, Erlangen, Germany) with phased-array coil systems. A multicomponent CMR that included evaluation of cardiac function by cine-CMR, myocardial viability using standard delayed enhancement (DE) CMR, and contrast-enhanced MRA to evaluate pulmonary venous anatomy were performed in all patients. Evaluation for LA/LAA thrombus was conducted by the following CMR components: 1) cine-CMR of the left atrium and LAA in at least 2 orthogonal views using a steady-state free-precession sequence with typical repetition time of 3.0 to 3.5 ms, echo time of 1.2 to 1.3 ms, in-plane spatial resolution of 2.0 × 1.6 mm, slice thickness of 6 mm, and temporal resolution of 35 to 40 ms; 2) nongated, contrast-enhanced 3-dimensional MRA during infusion of gadopentetate dimeglumine 0.15 mmol/kg, with image acquisition triggered when contrast was visualized in the left atrium (arterial phase) using a gradient echo sequence with flip angle of 25° to 40°, repetition time of 2.4 to 2.9 ms, echo time of 0.8 to 1.1 ms, in-plane spatial resolution of 1.5 × 1.3 mm, and slice thickness of 1.5 mm (typical breath-holding time of 10 to 12 s); and 3) single-shot inversion recovery, steady-state free-precession, multislice (covering entire left atrium and LAA in 2 orthogonal planes), equilibrium phase DE obtained approximately 10 min after intravenous gadolinium contrast administration using long inversion time (TI) set at 600 ms (long TI DE-CMR) to null avascular tissue with in-plane spatial resolution of 2.1 × 1.6 mm, and slice thickness of 4 mm without gap. Breath-holding was not required for the long TI DE-CMR sequence because each image was acquired during mid-diastole within a single heartbeat.

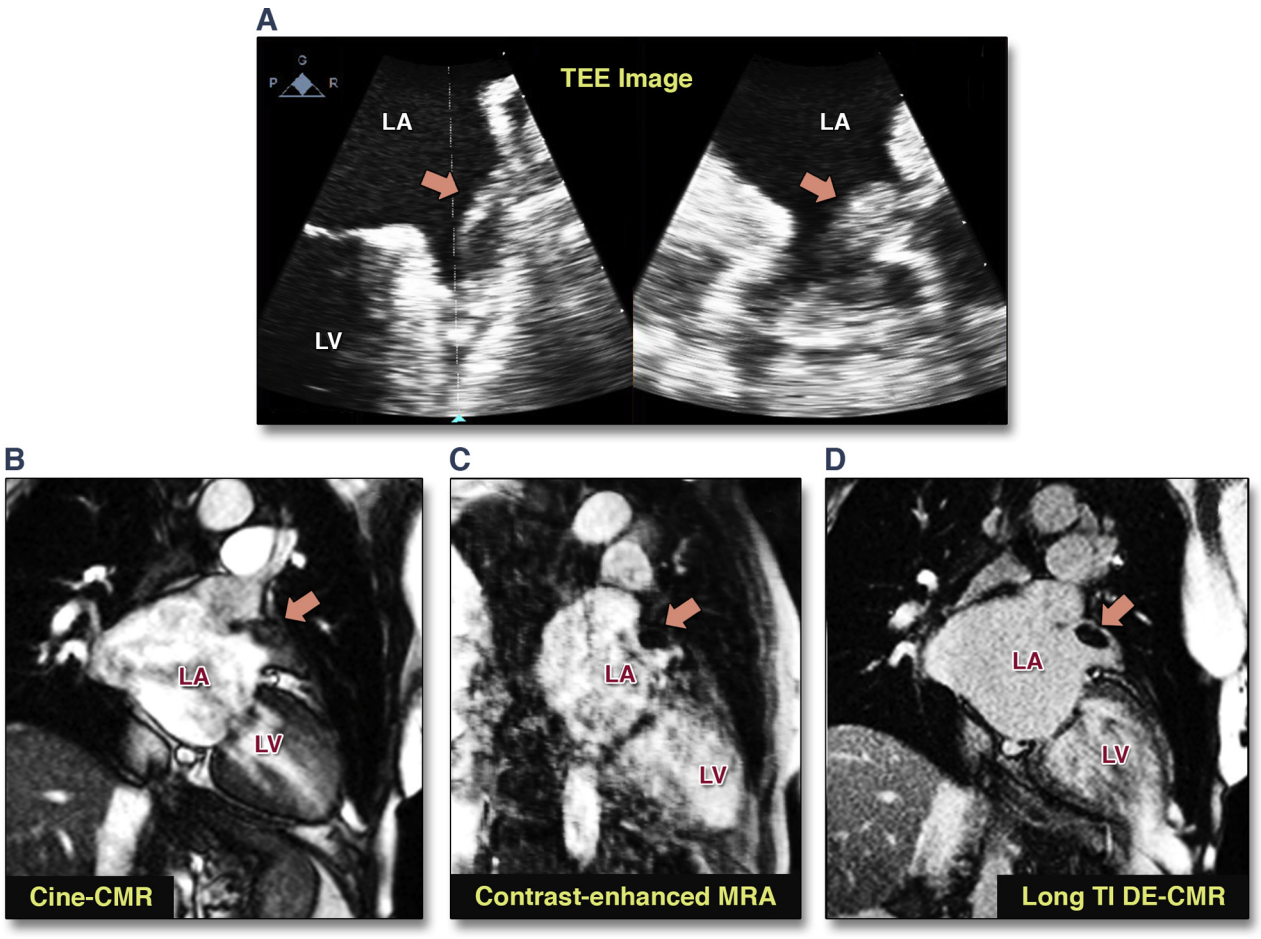
Briefly, left and right ventricular volumes were measured by planimetry of the endocardial borders on a stack of short-axis images acquired from breath-hold steady-state free-precession cines covering both ventricles, from base to apex, 1 slice per breath-hold. Papillary muscles and trabeculae were excluded from the blood pool on the contours. Left and right ventricular end-diastolic and end-systolic volumes were calculated by summation of these images. Left and right ventricular ejection fractions were determined

by subtracting the end-systolic volumes from the end-diastolic volumes and dividing the result by the end-diastolic volumes (14). The LA volume was calculated according to the bi-plane method using the LA area from 4- and 2-chamber long-axis images.

TEE PROTOCOL. TEE was performed with a 2- or 3-dimensional multiplane TEE probe by qualified cardiologists who had COCATS level III training in echocardiography. After the TEE probe was properly positioned in the mid-esophagus, the examination of the left atrium and LAA was performed according to the TEE guidelines from the American Society of Echocardiography (15). The left atrium and LAA were thoroughly investigated for thrombi in multiplane angles with particular attention to delineate the pectinate muscles from thrombus. Prolonged observation in a single plane or using simultaneous multiple-plane imaging was performed to differentiate sludge or spontaneous echocardiographic contrast from thrombus.

DEFINITION OF LA AND LAA THROMBUS. According to TEE, thrombus was defined as a well-circumscribed, highly reflective mass of uniform consistency, with texture different from the atrial wall and with a border distinct from the surrounding structures (15). Spontaneous echocardiographic contrast ("a smoke-like'' appearance, not well circumscribed, and without a uniform consistency) was not considered as thrombus. Thrombus was classified as mural thrombus if the borders were contiguous with adjacent LA or LAA contours. Thrombus size was measured in its largest dimension.

FIGURE 1 Example of Thrombus in LAA



Thrombus in the left atrial appendage (LAA) **(arrow)** detected by **(A)** transesophageal echocardiography (TEE), **(B)** cine-cardiac magnetic resonance (CMR), **(C)** contrast-enhanced magnetic resonance angiography (MRA), and **(D)** the equilibrium phase delayed enhancement CMR using a long inversion time of 600 ms (long TI DE-CMR). Images refer to subject #4 in Table 2. LA = left atrium; LV = left ventricle.

TABLE 1 Baseline Characteristics and CMR Findings of Study Population

	Total (n = 261)	Thrombus Present (n = 9)	Thrombus Absent (n = 252)	p Value
Clinical parameters				
Age, yrs	61.8 ± 11.8	58.8 ± 11.8	62.0 ± 11.9	0.429
Male	181 (69.4)	4 (44.4)	177 (70.2)	0.138
Body surface area, kg/m^2	2.1 ± 0.3	2.1 ± 0.4	2.1 ± 0.3	0.99
Time between CMR and TEE, days	1.3 ± 2.3	1.6 ± 2.4	1.2 ± 2.3	0.609
Heart failure	53 (20.3)	5 (55.6)	48 (19.0)	0.019
Hypertension	179 (68.6)	6 (66.7)	173 (68.7)	0.99
Diabetes	49 (18.8)	3 (33.3)	46 (18.3)	0.376
Coronary artery disease	51 (19.5)	4 (44.4)	47 (18.7)	0.076
History of stroke or TIA	24 (9.2)	0 (0.0)	24 (9.5)	
Paroxysmal AF	150 (57.5)	3 (33.3)	147 (58.3)	0.176
AF during CMR procedure	109 (41.8)	5 (55.6)	104 (41.2)	0.497
CHA_2DS_2VASc score				
<2	89 (34.1)	1 (11.1)	88 (34.9)	0.173
2–3	107 (41.0)	5 (55.6)	102 (40.5)	0.494
>3	65 (24.9)	3 (33.3)	62 (24.6)	0.695
Anticoagulation use	192 (73.6)	7 (77.8)	185 (73.4)	0.99
Antiplatelet use	80 (30.7)	3 (33.3)	77 (30.6)	0.99
CMR findings				
LVEDV index, ml/m^2	67.4 ± 20.8	75.7 ± 36.8	67.1 ± 20.1	0.224
RVEDV index, ml/m^2	69.3 ± 22.5	62.2 ± 26.6	69.6 ± 22.4	0.334
Left atrial volume index, ml/m^2	60.8 ± 23.9	75.5 ± 46.4	60.2 ± 22.7	0.059
LV ejection fraction, %	59.0 ± 13.6	49.4 ± 22.6	59.4 ± 13.1	0.030
RV ejection fraction, %	50.4 ± 9.9	41.8 ± 10.6	50.7 ± 9.8	0.008
LV mass index, g/m^2	68.1 ± 20.8	72.3 ± 20.9	68.0 ± 20.8	0.543

Values are mean ± SD or n (%). Values of $p < 0.05$ indicate statistical significance. Normal values for variables as follows: LVEDV index = 57 to 105 ml/m^2 for men and 56 to 96 ml/m^2 for women; RVEDV index = 61 to 121 ml/m^2 for men and 48 to 112 ml/m^2 for women; LA volume index = 26 to 52 ml/m^2 for men and 27 to 53 ml/m^2 for women; LV ejection fraction = 57% to 77%; RV ejection fraction = 52% to 72%; LV mass index = 49 to 85 g/m^2 for men and 41 to 81 g/m^2 for women (18).

AF = atrial fibrillation; CHA_2DS_2VASc = congestive heart failure, hypertension, ≥75 years of age, diabetes mellitus, stroke/transient ischemic attack, vascular disease, 65 to 74 years of age, sex category; CMR = cardiac magnetic resonance; LV = left ventricular; LVEDV = left ventricular end-diastolic volume; RV = right ventricular; RVEDV = right ventricular end-diastolic volume; TEE = transesophageal echocardiography; TIA = transient ischemic attack.

For cine-CMR, thrombus was defined as a mass within the LA or LAA cavity that had margins distinct from the LA or LAA wall and distinguishable from pectinate muscles or technical artifact (9). Using contrast-enhanced MRA, a low signal intensity filling defect in the left atrium or LAA that had borders discrete from surrounding structures or blood pool was interpreted as thrombus (13). Thrombus was diagnosed on long TI DE-CMR as a mass with post-contrast characteristics consistent with avascular tissue (9). Typically, thrombus appeared as homogeneously black on long TI DE-CMR surrounded by high signal intensity structures of blood pool cavity.

All TEE and CMR studies were interpreted by 2 readers who have COCAT level III training in TEE and CMR. All readers were blinded to clinical history and results of other imaging studies. Individual CMR components were evaluated separately and in random order. Using consensus of the 2 readers, CMR and TEE were classified to "thrombus" or "no thrombus" in the left atrium and LAA. The CMR study was identified as "possible thrombus" when LA or LAA thrombus could not be excluded. Specifically, for contrast-enhanced MRA, the study would not be interpreted as abnormal when thrombus could be excluded due to incomplete contrast opacification of the left atrium or LAA; rather, it would be classified as "possible thrombus." Figure 1 displays an example of an LAA thrombus detected by using TEE and multicomponent CMR in the same patient.

STATISTICAL ANALYSIS. All data are presented as mean ± SD for continuous variables and frequency or median with interquartile ranges for categorical variables. Patients with and without thrombus were compared using an unpaired Student *t* test for continuous variables and the Fisher exact test for categorical variables. Diagnostic performance of each CMR component (including sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy with 95% confidence intervals [CIs]) were calculated in a standard manner. To determine the diagnostic performance of each CMR component, using rational intention to exclude thrombus, the studies categorized as possible thrombus were included in the thrombus group for further analysis. Interobserver agreement for thrombus identification was calculated using the kappa coefficient. Values of $p < 0.05$ were considered statistically significant.

RESULTS

During the study period, 261 multicomponent CMR studies met the inclusion criteria and were included for further analysis. The patient baseline characteristics are summarized in Table 1. The majority of the patients in the study cohort were male (69.4%), with a mean age of 61.8 ± 11.8 years. Hypertension was the most common comorbidity (68.6%), and 24 patients (9.2%) had a history of stroke or transient ischemic attack. AF was recorded as the cardiac rhythm during the CMR procedure in 109 patients (41.8%). The cardiac rhythm at the time of CMR and TEE were different in 7 patients: 3 patients were in AF during the time of CMR but in sinus rhythm at the time of TEE, and 4 patients were in sinus rhythm at the time of CMR but in AF during the TEE procedure. Of note, thrombus was not detected by CMR or TEE in any of these patients. The median CHA_2DS_2VASc score was 2 (interquartile range: 1 to 3). Anticoagulation use was reported in 192 patients (73.6%) during the time of CMR examination. In our institution, a patient who is undergoing anticoagulation therapy will be

continued on therapeutic anticoagulation throughout the pre-procedural period until the day of the PVI procedure.

CMR findings are shown in **Table 1**. Left and right ventricular size and systolic function were noted to be within normal range. However, the mean LA volume index (60.8 ± 23.9 ml/m^2) was increased in the study cohort. The patients with presence of LA/LAA thrombus had higher prevalence of heart failure and lower left and right ventricular ejection fraction compared with those without. In patients with LA/LAA thrombus, the median CHA_2DS_2VASc score was 3.

There were no complications from TEE or CMR noted for the study patients. According to TEE, LA and LAA thrombi were detected in 9 studies (3.5%) as shown in **Table 2**. Thrombi were found in the LAA in 7 studies (2.7%) and in the left atrium in 2 studies (0.8%). Long TI DE-CMR was able to identify all cases of thrombi detected by using TEE. Cine-CMR could not identify thrombi in 3 studies in which all LAA thrombus size was found to be ≤0.9 cm according to TEE. Contrast-enhanced MRA was not able to detect thrombus in 3 studies (2 laminated mural LA thrombi and 1 LAA thrombus). **Figures 2 and 3** illustrate example cases that long TI DE-CMR could correctly identify thrombus in the left atrium or LAA, whereas the other investigated CMR components could not. Of 9 patients initially found to have thrombus according to TEE, 5 underwent PVI after anticoagulation therapy; repeated imaging (3 had repeat CMR) demonstrated no evidence of thrombus in the left atrium or LAA. Among the 249 patients (95.4%) who subsequently underwent PVI (including 5 patients previously identified with thrombus), no stroke or transient ischemic attack was reported post-procedure.

The interobserver agreement was highest in long TI DE-CMR (kappa = 0.91; 95% CI: 0.78 to 1.0) followed by cine-CMR (kappa = 0.85; 95% CI: 0.74 to 0.97) and contrast-enhanced MRA (kappa = 0.83; 95% CI: 0.69 to 0.98). Diagnostic performance of LA/LAA thrombus detection by each CMR component is demonstrated in **Figure 4**. Among CMR sequences investigated in the study, long TI DE-CMR had the best diagnostic accuracy (99.2%; 95% CI: 97.2% to 99.9%), sensitivity (100%; 95% CI: 66.4% to 100%), specificity (99.2%; 95% CI: 97.2% to 99.9%), positive predictive value (81.8%; 95% CI: 48.2% to 97.7%), and negative predictive value (100%; 95% CI: 98.5% to 100%). In contrast, cine-CMR had the lowest diagnostic accuracy of 91.6% (95% CI: 87.5% to 94.6%), sensitivity of 66.7% (95% CI: 29.9% to 2.5%), specificity of 92.5% (95% CI: 88.5% to 95.4%), and a

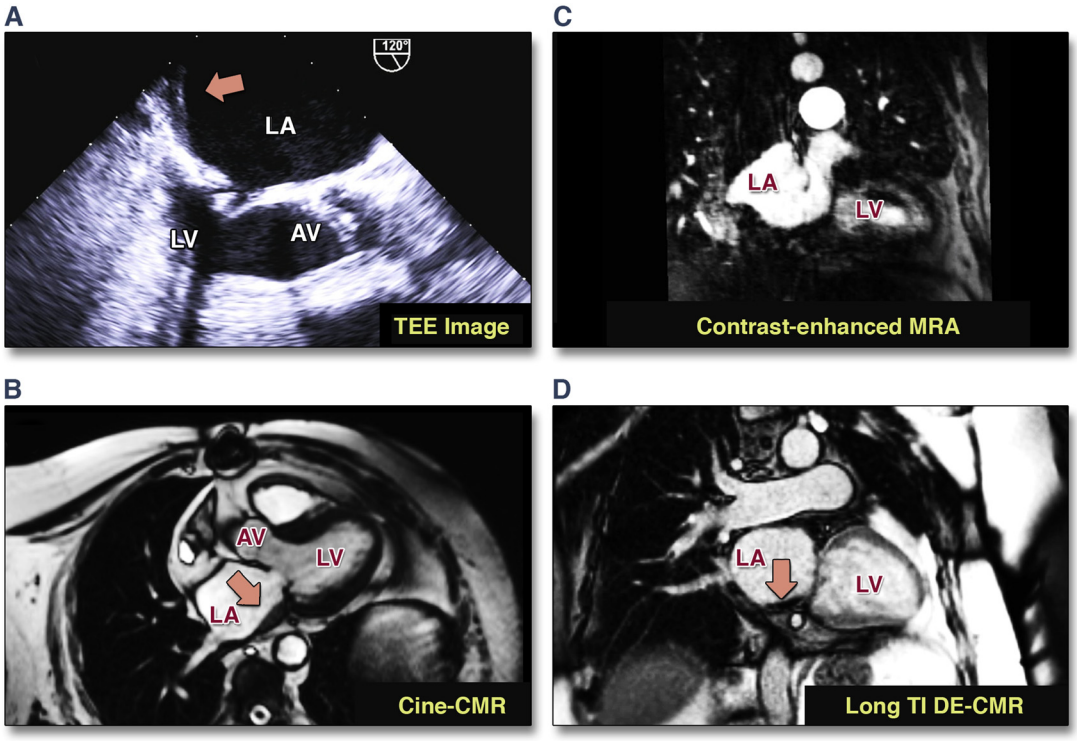
TABLE 2 Clinical Characteristics and CMR Performance in Patients With LA or LAA Thrombus Detected by Using TEE or Long TI DE-CMR

Subject #	Age (yrs)	Sex	CHA_2DS_2VASc Score	Valvular Status	Anticoagulation Therapy	Time Between CMR and TEE (days)	Rhythm at CMR	LVEF (%)	LA Volume Index (ml/m^2)	CMR Strength	Location of Thrombus	Thrombus Size by TEE* (cm)	Thrombus Size by CMR* (cm)	CMR Components		
														Cine-CMR	MRA	Long TI DE-CMR
1	71	F	4	Prosthetic MV ring	Warfarin	0	AF	77	54.5	1.5-T	LA (mural)	1.8	1.6	+	-	+
2	72	F	4	Prosthetic MV ring	Dabigatran	3	AF	66	65.2	1.5-T	LA (mural)	2.3	2.2	+	-	+
3	41	M	1	None	No	1	AF	29	77.8	1.5-T	LAA	2.5	2.3	+	+	+
4	68	F	4	Moderate MR and AV bioprosthesis	Warfarin	0	SR	58	194.3	1.5-T	LAA	2.1	1.6	+	+	+
5	44	F	3	Mechanical MV	Warfarin	0	SR	31	64.7	1.5-T	LAA	1.1	1.4	+	+	+
6	54	F	2	None	No	0	SR	84	32.1	3-T	LAA	0.9	1.2	-	+	+
7	69	M	3	None	Warfarin	0	SR	45	70.1	3-T	LAA	0.7	0.7	-	+	+
8	52	M	3	None	Warfarin	3	AF	26	64.5	1.5-T	LAA	0.6	0.6	-	+	+
9	58	M	3	None	Warfarin	7	AF	29	56.0	3-T	LAA	0.6	0.5	±	-	+
10†	77	M	4	None	Warfarin	3	AF	55	68.9	1.5-T	LAA	None	0.6	-	±	±
11†	53	M	3	None	Warfarin	3	AF	36	61.3	1.5-T	LAA	None	0.5	±	-	±

Normal values for LVEF and LA volume index as detailed in Table 1. *Thrombus size was measured from its largest dimension by using TEE and long TI DE-CMR. †Unlike in subjects #1 through #9, thrombus was not detected by TEE in subjects #10 and #11, resulting in a false-positive interpretation by long TI DE-CMR.

+ = thrombus; - = no thrombus; ± = possible thrombus; AV = aortic valve; F = female; LA = left atrial; LAA = left atrial appendage; TI DE-CMR = equilibrium phase delayed enhancement CMR using long inversion time of 600 ms; LVEF = left ventricular ejection fraction; MRA = magnetic resonance angiography; M = male; MR = mitral regurgitation; MV = mitral valve; SR = sinus rhythm; other abbreviations as in Table 1.

FIGURE 2 Example of Mural Thrombus in the Posterior LA Wall



Laminated mural thrombus in the posterior left atrial (LA) wall **(arrow)** detected by **(A)** TEE, **(B)** cine-CMR, and **(D)** long TI DE-CMR. **(C)** Contrast-enhanced MRA was not able to identify this mural thrombus. Images refer to subject #2 in Table 2. Abbreviations as in Figure 1.

positive predictive value of 24% (95% CI: 9.4% to 45.1%). All of the CMR sequences had a high negative predictive value, ranging from 98.7% by cine-CMR to 100% by long TI DE-CMR. Cine-CMR and contrast-enhanced MRA were not able to exclude LA/LAA thrombus, resulting in a possible thrombus interpretation in 18 studies (6.9%) and 12 studies (4.6%), respectively, whereas 2 studies (0.8%) were interpreted as possible thrombus according to long TI DE-CMR.

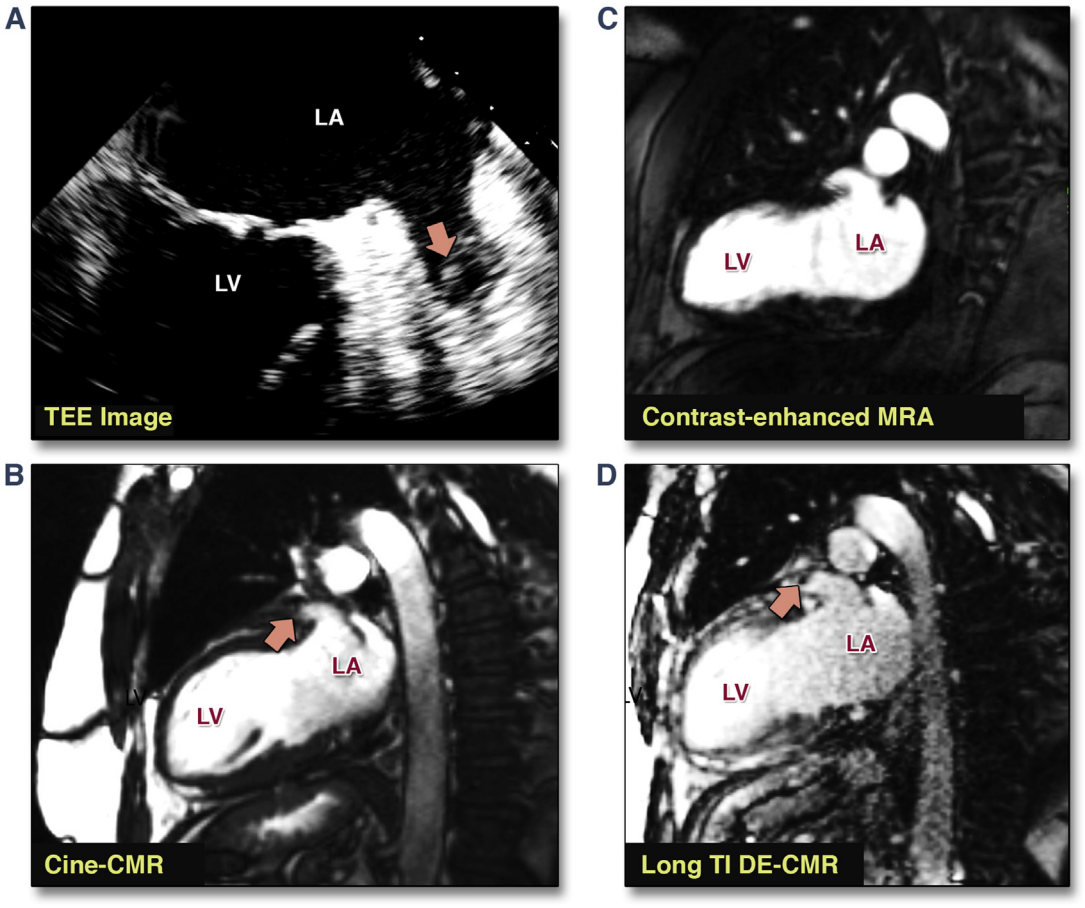
In our investigation, 143 studies (54.8%) were performed on a 3-T scanner, and 118 studies (45.2%) were performed on a 1.5-T scanner. The diagnostic accuracy of the investigated CMR components performed by using the 3- or 1.5-T scanners was not significantly different, and long TI DE-CMR remains the CMR component that has the highest diagnostic accuracy on both scanners (99.3% [3-T] vs. 99.1% [1.5-T]; $p = 0.99$) followed by contrast-enhanced MRA (95.8% [3-T] vs. 92.4% [1.5-T]; $p = 0.289$) and cine-CMR (93.0% [3-T] vs. 89.8% [1.5-T]; $p = 0.379$). Although the diagnostic accuracy of long TI DE-CMR (98.2% [AF] vs. 100% [no AF]; $p = 0.174$), contrast-enhanced MRA (93.6% [AF] vs. 94.7% [no AF]; $p = 0.789$), and cine-CMR (88.1% [AF] vs. 94.1% [no AF]; $p = 0.113$) in patients with AF during the time of the CMR procedure was less than in those without AF, the findings were not statistically significant.

DISCUSSION

Our study is the largest investigation to date to evaluate the utility of CMR in assessment of LA/LAA thrombus in patients referred for PVI. The result of our study showed that multicomponent CMR is a feasible diagnostic modality for assessment of LA/LAA thrombus. For patients referred for PVI, multicomponent CMR can be a single comprehensive study that provides pulmonary venous anatomy mapping and simultaneously evaluates the presence of thrombus in the left atrium or LAA. This finding could potentially reduce the amount of pre-operative testing and overall procedure cost for patients referred for PVI.

Despite the high negative predictive value for LA/LAA thrombus detection found in all investigated

FIGURE 3 Example of Small LAA Thrombus



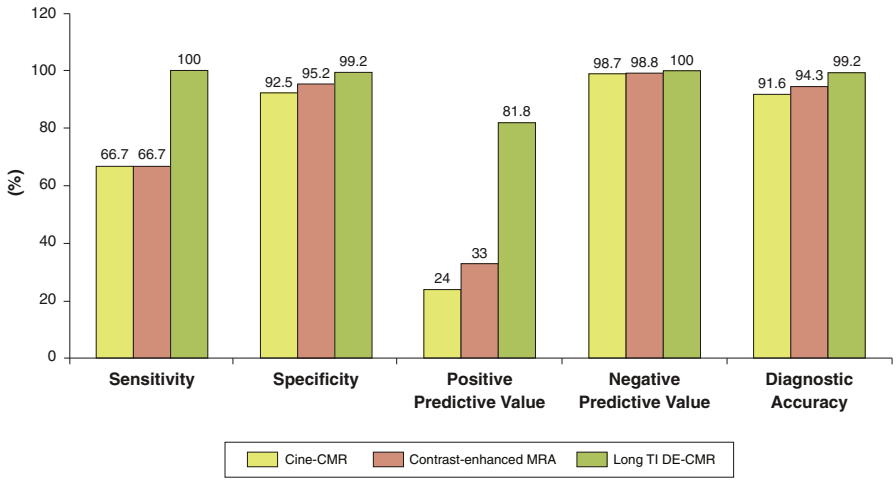
Example of small LAA thrombus **(arrow)** detected by **(A)** TEE and **(D)** long TI-DE-CMR. LAA thrombus could not be excluded by **(B)** cine-CMR, whereas **(C)** contrast-enhanced MRA failed to identify LAA thrombus. Images refer to subject #9 in Table 2. Abbreviations as in Figure 1.

CMR components, the diagnostic performance of long TI DE-CMR was superior to other CMR components and was not affected by the use of a 1.5- or 3-T scanner or the presence of AF at the time of the CMR procedure. For assessment of thrombus, long TI DE-CMR can provide additional advantages over standard DE-CMR as shown in a previous study (9). Weinsaft et al. (9) validated the ability of long TI DE-CMR for detection of left ventricular thrombus and also showed the superiority of this technique over cine-CMR. Similar to this study in which cine-CMR generally missed small left ventricular thrombus, cine-CMR in our study was not able to identify the presence of thrombus in studies with small LAA thrombi.

CMR protocols used for the evaluation of LA/LAA thrombus in previous studies carried certain limitations. Double and triple inversion recovery sequences are susceptible to flow-related enhancement artifacts that can interfere with LA and LAA thrombus evaluation (12). The 2-dimensional CMR perfusion is limited by spatial resolution and imaging plane during perfusion (13). Spatial resolution and image contrast between background and LA/LAA wall, as well as slow flow in the left atrium and LAA, can affect evaluation of thrombus by 3-dimensional contrast-enhanced CMR (11,13). Imaging artifacts are also commonly encountered in cine-CMR; these include breathing motion, flow-related, and inhomogeneity artifacts (16). Accordingly, in our study, thrombus could not be excluded by using cine-CMR and contrast-enhanced MRA in a number of patients. These were caused by flow-related and inhomogeneity artifacts in the majority of cine-CMR studies, whereas underfilled LAA due to sluggish flow in LA and LAA were typically seen in contrast-enhanced MRA. Long TI DE-CMR provided

FIGURE 4 Diagnostic Performance of Each CMR Component

	TEE (n = 261)	Cine CMR (n = 261)	Contrast-enhanced MRA (n = 261)	Long TI DE-CMR (n = 261)
Thrombus	9 (3.5%)	7 (2.7%)	6 (2.3%)	9 (3.5%)
No Thrombus	252 (96.5%)	236 (90.4%)	243 (93.1%)	250 (95.8%)
Possible Thrombus	0	18 (6.9%)	12 (4.6%)	2 (0.8%)

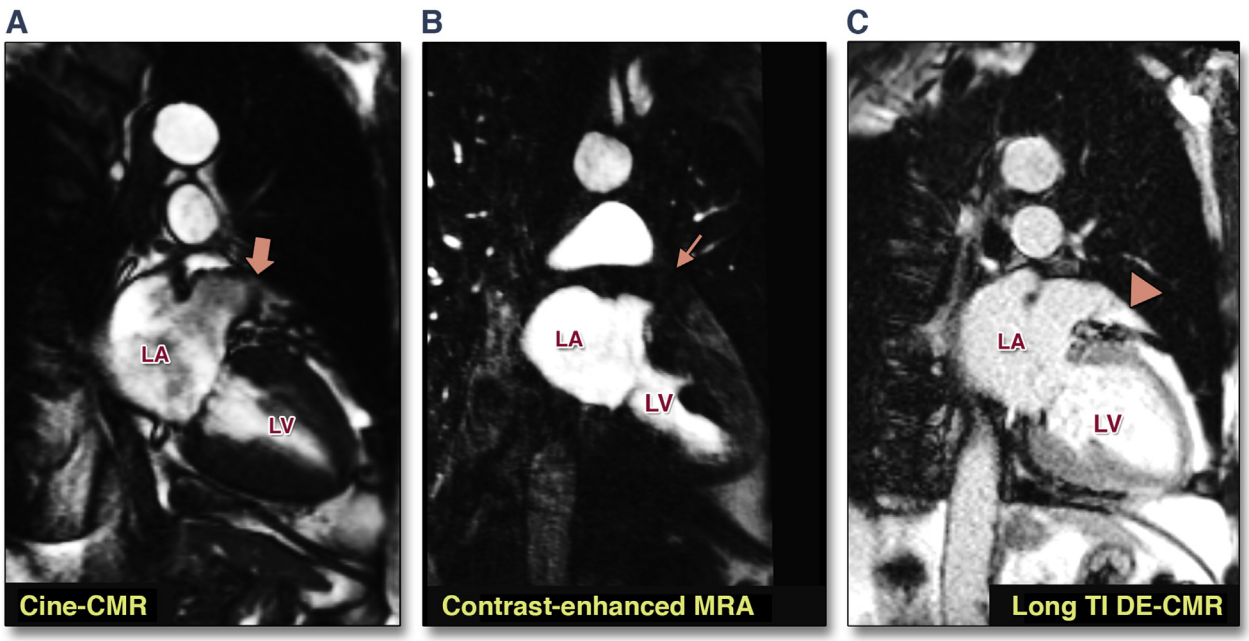


Long TI DE-CMR was able to identify all thrombus detected by TEE. Despite a high negative predictive value, cine-CMR and contrast-enhanced MRA could not exclude thrombus in 6.9% and 4.6%, respectively, resulting in a low positive predictive value. Long TI DE-CMR had the highest diagnostic performance for detection of LA/LAA thrombus in all categories compared with other CMR components. Abbreviations as in Figure 1.

advantages over other CMR components in multiple ways. Figure 5 illustrates a case with no LA/LAA thrombus documented by TEE, but only long DE-CMR could exclude the presence of thrombus while other investigated CMR components could not. Multislice, long TI DE-CMR provided adequate coverage of the entire left atrium and LAA, but it is less susceptible to artifact and could prevent the situation of underfilled LAA because it was performed with a single-shot technique in the equilibrium phase, 10 min after contrast administration. In addition, due to the rapid acquisition time of this technique, breath-holding was not required; it could also be performed in the setting of irregular cardiac rhythm, which might be encountered in patients with AF before PVI. As shown in our analysis, long TI DE-CMR had only a few studies in which LA/LAA thrombus could not be excluded, resulting in a better positive predictive value and diagnostic performance than the other CMR components. In fact, in our study, findings from cine-CMR and contrast-enhanced MRA provided no further information regarding LA/LAA thrombus assessment in addition to what long TI DE-CMR had already provided. With these available data, long TI DE-CMR is the preferable CMR sequence and should be used for LA/LAA thrombus detection.

To our knowledge, there is no previous study directly comparing cardiac CT and CMR scans for LA/LAA thrombus detection in this clinical setting. The longer time required for CMR examination has been commonly criticized as a disadvantage of CMR. In fairness, if the CMR protocols were tailored to evaluate pulmonary venous anatomy and identify LA/LAA thrombus, the image acquisition time could be significantly reduced, although not as short as in cardiac CT scans. In contrast to cardiac CT scanning, CMR could provide valuable data for PVI procedures without exposure to radiation. This scenario might be even more important in certain patients who are expected to have a long PVI procedure time or a repeat procedure in the future. The criteria in cardiac CT scanning that are used to determine the presence of thrombus rely on detection of low attenuation regions, which can occasionally can be difficult to differentiate from sluggish blood flow in the left atrium/LAA that may be seen in patients with AF (6). Tissue characterization is a unique advantage of CMR that provides further information in thrombus assessment and would not be affected by slow flow in the left atrium or LAA. In addition, the extent of LA fibrosis or scarring can be assessed by DE-CMR and may be of value in selected patients (4).

FIGURE 5 Example of Normal Study Without Thrombus Detected by TEE



In this example, no thrombus was identified by TEE. LAA thrombus could not be excluded by **(A)** cine-CMR due to flow-related artifact in the LAA **(arrow)** and by **(B)** contrast-enhanced MRA due to underfilled LAA **(thin arrow)**; however, with **(C)** long TI DE-CMR, LAA **(arrowhead)** can be clearly visualized and without the presence of thrombus. Abbreviations as in Figure 1.

STUDY LIMITATIONS. Similar to cardiac CT scanning, the diagnostic performance of contrast-enhanced MRA was affected by underfilled LAA, which complicated differentiation between thrombus and sluggish blood flow (6). Cardiac CT scans with delayed images (typically 30 to 180 s after contrast injection) has been shown to improve the diagnostic accuracy of LA/LAA thrombus detection from 90% to 99%. Likewise, using delayed contrast-enhanced MRA images may help improve diagnostic accuracy for LA/LAA thrombus detection with this technique. The utility of phase sensitive inversion recovery DE-CMR was not evaluated in our study. It should be noted that with a routine DE-CMR utilizing a TI set to null myocardium, thrombus may appear grey with a black rim on magnitude images; however, with phase-sensitive inversion recovery DE-CMR that reconstructed and discriminated positive and negative signal amplitude, thrombus appear black and is easy to identify. The phase-sensitive inversion recovery sequence could potentially be another method of thrombus imaging that does not require additional TI adjustment. Unlike TEE that could provide both anatomical and physiological data such as LAA emptying velocity, the CMR components evaluated in our study could only provide anatomical data (17). It is known that prevalence can affect diagnostic performance of a test and therefore the performance characteristics of the CMR components in our study needs to be interpreted with this fact in mind. However, multiple studies using cardiac CT scanning to evaluate LA/LAA thrombus with TEE as the reference standard in the setting of PVI demonstrated an incidence/prevalence of LA/LAA thrombus of 2% to 19% (6), which appears in line with our data, thus supporting the generalizability of our findings. Despite being the largest study to evaluate the diagnostic performance of CMR in assessing LA/LAA thrombus, the results of our study reflect the experience from a single center. Further multicenter studies with larger sample sizes are necessary to confirm our findings.

CONCLUSIONS

In patients referred for PVI, CMR is a noninvasive test that has a favorable diagnostic performance and could be an alternative imaging modality to TEE for assessment of LA/LAA thrombus. In our study, long TI DE-CMR was shown to be the most reliable CMR

sequence and should be used for LA/LAA thrombus detection. CMR may be a single comprehensive diagnostic study to assess pulmonary venous anatomy as well as the presence of LA/LAA thrombus, thus potentially reducing the number of pre-operative tests before PVI.

REPRINT REQUESTS AND CORRESPONDENCE: Dr. Dipan J. Shah, Houston Methodist DeBakey Heart & Vascular Center, 6550 Fannin Street, Smith Tower, Suite 677, Houston, Texas 77030. E-mail: djshah@houstonmethodist.org.

PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: CMR may be a comprehensive test for evaluation of pulmonary venous anatomy and LA/LAA thrombus in patients referred for PVI.

TRANSLATIONAL OUTLOOK: Future multicenter studies are needed to confirm the utility of CMR as a comprehensive test before the PVI procedure.

REFERENCES

1. January CT, Wann LS, Alpert JS, et al. 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. J Am Coll Cardiol 2014;64:e1–76.

2. Chugh SS, Havmoeller R, Narayanan K, et al. Worldwide epidemiology of atrial fibrillation: a Global Burden of Disease 2010 Study. Circulation 2014;129:837–47.

3. Iwasaki YK, Nishida K, Kato T, Nattel S. Atrial fibrillation pathophysiology: implications for management. Circulation 2011;124:2264–74.

4. Calkins H, Kuck KH, Cappato R, et al. 2012 HRS/EHRA/ECAS expert consensus statement on catheter and surgical ablation of atrial fibrillation: recommendations for patient selection, procedural techniques, patient management and follow-up, definitions, endpoints, and research trial design: a report of the Heart Rhythm Society (HRS) Task Force on Catheter and Surgical Ablation of Atrial Fibrillation. Developed in partnership with the European Heart Rhythm Association (EHRA), a registered branch of the European Society of Cardiology (ESC) and the European Cardiac Arrhythmia Society (ECAS); and in collaboration with the American College of Cardiology (ACC), American Heart Association (AHA), the Asia Pacific Heart Rhythm Society (APHRS), and the Society of Thoracic Surgeons (STS). Heart Rhythm 2012;9:632–96.e21.

5. Manning WJ, Weintraub RM, Waksmonski CA, et al. Accuracy of transesophageal echocardiography for identifying left atrial thrombi. A prospective, intraoperative study. Ann Intern Med 1995;123:817–22.

6. Romero J, Husain SA, Kelesidis I, Sanz J, Medina HM, Garcia MJ. Detection of left atrial appendage thrombus by cardiac computed tomography in patients with atrial fibrillation: a meta-analysis. Circ Cardiovasc Imaging 2013;6:185–94.

7. Kim SC, Chun EJ, Choi SI, et al. Differentiation between spontaneous echocardiographic contrast and left atrial appendage thrombus in patients with suspected embolic stroke using two-phase multidetector computed tomography. Am J Cardiol 2010;106:1174–81.

8. Hundley WG, Bluemke DA, Finn JP, et al. ACCF/ACR/AHA/NASCI/SCMR 2010 expert consensus document on cardiovascular magnetic resonance: a report of the American College of Cardiology Foundation Task Force on Expert Consensus Documents. J Am Coll Cardiol 2010;55:2614–62.

9. Weinsaft JW, Kim HW, Shah DJ, et al. Detection of left ventricular thrombus by delayed-enhancement cardiovascular magnetic resonance prevalence and markers in patients with systolic dysfunction. J Am Coll Cardiol 2008;52:148–57.

10. Srichai MB, Junor C, Rodriguez LL, et al. Clinical, imaging, and pathological characteristics of left ventricular thrombus: a comparison of contrast-enhanced magnetic resonance imaging, transthoracic echocardiography, and transesophageal echocardiography with surgical or pathological validation. Am Heart J 2006;152:75–84.

11. Rathi VK, Reddy ST, Anreddy S, et al. Contrast-enhanced CMR is equally effective as TEE in the evaluation of left atrial appendage thrombus in patients with atrial fibrillation undergoing pulmonary vein isolation procedure. Heart Rhythm 2013;10:1021–7.

12. Ohyama H, Hosomi N, Takahashi T, et al. Comparison of magnetic resonance imaging and transesophageal echocardiography in detection of thrombus in the left atrial appendage. Stroke 2003;34:2436–9.

13. Mohrs OK, Nowak B, Petersen SE, et al. Thrombus detection in the left atrial appendage using contrast-enhanced MRI: a pilot study. AJR Am J Roentgenol 2006;186:198–205.

14. Schulz-Menger J, Bluemke DA, Bremerich J, et al. Standardized image interpretation and post processing in cardiovascular magnetic resonance: Society for Cardiovascular Magnetic Resonance (SCMR) board of trustees task force on standardized post processing. J Cardiovasc Magn Reson 2013;15:35.

15. Hahn RT, Abraham T, Adams MS, et al. Guidelines for performing a comprehensive transesophageal echocardiographic examination: recommendations from the American Society of Echocardiography and the Society of Cardiovascular Anesthesiologists. J Am Soc Echocardiogr 2013;26:921–64.

16. Ferreira PF, Gatehouse PD, Mohiaddin RH, Firmin DN. Cardiovascular magnetic resonance artefacts. J Cardiovasc Magn Reson 2013;15:41.

17. Zabalgoitia M, Halperin JL, Pearce LA, Blackshear JL, Asinger RW, Hart RG. Transesophageal echocardiographic correlates of clinical risk of thromboembolism in nonvalvular atrial fibrillation. Stroke Prevention in Atrial Fibrillation III Investigators. J Am Coll Cardiol 1998;31:1622–6.

18. Kawel-Boehm N, Maceira A, Valsangiacomo-Buechel ER, et al. Normal values for cardiovascular magnetic resonance in adults and children. J Cardiovasc Magn Reson 2015;17:29.

KEY WORDS atrial fibrillation, cardiovascular MRI, left atrial appendage, pulmonary vein isolation, thrombus