Value of Cardiac Cine MRI in Comparison to Contrast Transcranial Doppler Sonography for Patent Foramen Ovale Assessment in Patients with Cerebral Disorders

Zhiming Li
The Affiliated Hospital of Qingdao University
Shunli Liu
The Affiliated Hospital of Qingdao University
Tingfei Yan
The Affiliated Hospital of Qingdao University
Yabin Hu
The Affiliated Hospital of Qingdao University
Chuanyu Zhang
The Affiliated Hospital of Qingdao University
Zhiguo Ju
Shanghai University of Medicine and Health Sciences
Hongqin Zhao
The Affiliated Hospital of Qingdao University
Guangzhen Liu (liugzh5750@163.com)
The Affiliated Hospital of Qingdao University

Research Article

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Abstract

Purpose: To investigate the clinical feasibility of diagnosing and classifying patent foramen ovale (PFO) in patients with cerebral disorders by cardiac cine MRI (CCMRI) without contrast.

Materials and Methods: Forty-four patients (24 males and 20 females; mean age, 41.3 years; range, 21–64 years) with cerebral disorders underwent contrast transcranial Doppler sonography (cTCD) and non-enhanced CCMRI examinations between October 2019 and March 2020. CCMRI was performed with a 3.0T magnetic resonance (MR) scanner using the OBL FIESTA CINE 4CH sequence. The scanning direction was perpendicular to the interatrial septum (IAS). The obtained MR images were analyzed by AW station 4.4. Pseudo-color coding was performed based on the different phases. The blood shunt condition was observed and recorded, noting the PFO length and width and whether it was complicated by IAS aneurysm or secondary septum thickening.

Results: Thirty-nine of the 44 patients with cerebral disorders were confirmed to have right-to-left shunt by cTCD, and 37 of them were diagnosed with PFO by CCMRI. Two of the five remaining patients were also diagnosed with PFO by CCMRI. Compared with cTCD as a standard, CCMRI assessment resulted in the following: sensitivity, 94.9%; specificity, 60.0%; accuracy, 90.9%; positive predictive value, 94.9%; negative predictive value, 60.0%; area under the curve, 0.774. Using pseudo-color coding, a right-to-left color jet was observed in 34 patients, and a two-way shunt was found in five. IAS aneurysm and secondary septum thickening were found in five and three patients (11.4% and 6.8%), respectively. The maximum PFO diameters ranged from 1.7 to 16.8 mm, and the mean diameter was 5.4 ± 3.4 mm.

Conclusion: The noninvasive CCMRI without contrast proved an excellent method for PFO identification, evaluation, and classification, with high sensibility (92.85%) and concordance (90.9%) compared to cTCD.

Introduction

Patent foramen ovale (PFO) is a physiological channel in the atrial septum. Recent studies have found that the prevalence of PFO was higher in cryptogenic stroke patients than in the general population (54 vs. 25%) [1]. Therefore, PFO diagnosis would be crucial for patients with cryptogenic cerebral symptoms.

Transesophageal echocardiography (TEE) with bubble study is the gold standard for PFO diagnosis [2]. However, TEE is a semi-invasive technique and requires general sedation with its associated complication. Transthoracic echocardiography (TTE), contrast transcranial Doppler sonography (cTCD), and computed tomography (CT) are less invasive alternative imaging modalities with acceptable sensitivity in detecting PFO [3-5]. Among these, TTE depends heavily on the operator's work experience, and missed diagnoses are unavoidable. cTCD does not provide direct evidence for PFO detection and is easily disturbed by other right-to-left cardiac shunts at the atrial or ventricular level, such as ventricular septal defect (VSD) or intrapulmonary shunt [6]. Contrast-enhanced CT is limited by the ionizing radiation and the risk of contrast agent allergy.

Cardiac magnetic resonance imaging (CMRI) is a noninvasive imaging modality that provides detailed information on cardiac anatomy and function, and its utility has been established in many cardiovascular applications. Previously, several studies have focused on the feasibility of using contrast-enhanced CMRI for PFO detection and follow-up [7-9]. The sensitivity of 1.5T MRI for detecting PFO varied across studies (37.5–100%), using TEE with bubble as the reference standard. The diagnostic value of 3.0T MRI cine sequences compared with cTCD in detecting PFO has not been addressed.

This study aimed to investigate the clinical feasibility of using CMRI with cine sequences (CCMRI) to diagnose and assess PFO in patients with cerebral disorders.

Materials And Methods

Patient Selection

We retrospectively reviewed 66 patients with cerebral disorders admitted to our hospital from October 2019 to March 2020 and suspected of having PFO. The local ethics committee approved this study, and the requirement for informed consent was waived.

The inclusion criteria were as follows: (1) presented with cerebral disorders, such as migraine headache, visual-field defect, cerebral infarction, transient ischemic attack, or dizziness; (2) availability of CCMRI and cTCD examinations before treatment.

The exclusion criteria were as follows: (1) with a history of another cardiac disease, such as atrial fibrillation or valvular heart disease; (2) with carotid atherosclerosis or at high risk for small-vessel atherosclerosis due to comorbidities such as hypertension or diabetes [10]; (3) with obvious artifacts on the MR images.

Finally, 44 patients (mean age, 41.3 years; range, 21–64 years) were enrolled in our study.

MRI Scanning Protocol and the Post-processing Process

MRI examinations were performed on a 3.0T magnetic resonance (MR) scanner (Discovery MR750, GE Medical Systems). The data were acquired using a dedicated eight-element cardiac phased-array coil with vector-ECG gating. An OBL FIESTA CINE 4CH sequence served for detecting the PFO anatomy and dynamic shunting. The scanning direction was perpendicular to the interatrial septum (IAS). Image acquisition parameters were as follows: repetition time (TR), 3.3 ms; echo time (TE), 1.5 ms; slice thickness, 6 mm; matrix, 176 × 256; in-plane resolution, 2.1 × 1.6 mm; reconstructed voxel size, 1.5 × 1.5 × 6.0 mm. The obtained cardiac MR images were analyzed with a post-processing workstation software program (AW station 4.4, GE Medical Systems), and pseudo-color coding was performed based on the different phases.

Two independent reviewers (LZM and HYB, with 6 and 8 years of experience, respectively) performed all image interpretations to assess for right-to-left shunting (RLS), achieving consensus by discussion. The reviewers were blind to the cTCD findings. The right-to-left blood shunt condition was observed and recorded, noting the PFO length and width and whether it was complicated by interatrial septum (IAS) aneurysm or secondary septum thickening. IAS aneurysm was defined as maximal oscillation extent of the atrial septum >10 mm [8]. Secondary septum thickening was considered positive when the thickness exceeded 6 mm.

The cTCD Test

All cTCD studies were performed by a neurologist (ZHQ, with six years of experience) with a 2-MHz transducer (EMS-9A). The patients were in a supine position in a controlled temperature environment (24 to 28ºC). A fixed helmet was used to continuously measure the mean flow velocity in the middle cerebral arteries (MCA) through the temporal window. cTCD was performed according to the standardized consensus procedure [11]. Briefly, a 10 mL contrast of air-mixed saline (9 mL of normal saline solution and 1 mL of air) was injected into the right antecubital vein while resting and before performing the Valsalva maneuver (VM). The VM was performed five seconds after contrast injection, and its effectiveness was monitored by a 25% decrease of MCA flow velocity. All cTCD tests were repeated twice to avoid possible misinterpretations, with each test lasting one minute. An RLS was considered positive when five or more air microbubbles were detected on the spectral display within 20 seconds of the start of injection.

Statistical Analysis

With cTCD as the reference standard, we calculated the sensitivity, specificity, accuracy, positive predictive value (PPV), and negative predictive value (NPV) of CCMRI for detecting PFO. The findings by cTCD and CCMRI were compared by the Chi-squared test. The receiver operating characteristic (ROC) analysis evaluated the diagnostic performance. *P*-values smaller than 0.05 indicated significant differences. Statistical analysis was performed using IBM SPSS Statistics for Windows, Version 22.0 (IBM Corp., Armonk, NY, USA).

Results

Of the 44 patients with cerebral disorders, we found migraine headaches in 16, visual-field defects in ten, cerebral infarctions in seven, transient ischemic attacks in five, convulsions in three, and dizziness in three (Table 1).

Thirty-nine patients were positive for RLS based on cTCD, with no evidence of PFO in the remaining five patients.

PFO was diagnosed in 39 patients by reviewing the CCMRI sequences, of which 37 were positive for RLS in the cTCD test (Table 2). Two of the five patients negative for PFG in CCMRI were positive in the cTCD test, both with Grade 1 RLS (Table 3). Based on post-processing images, the right-to-left color jet was observed in 34 patients, and two-way shunting was found in five. Furthermore, IAS aneurysm and secondary septum thickening were found in five and three patients (11.4 and 6.8%), respectively. Channel-like and latticed appearances of the IAS were detected in six and two patients (13.6 and 4.5%), respectively. The maximum PFO diameters ranged from 1.7 to 16.8 mm, and the mean diameter was 5.4 ± 3.4 mm. Representative images are shown in Fig. 1.

When compared with cTCD as a standard for PFO detection, cCMRI without contrast had a sensitivity of 94.9%, a specificity of 60.0%, an accuracy of 90.9%, a PPV of 94.9%, an NPV of 60.0%, and an area under the curve (AUC) of 0.774.

Discussion

CCMRI without a contrast agent has not been used widely for PFO diagnosis in clinical practice due to its insufficient spatial and temporal resolutions. Previous studies have focused on contrast-enhanced MRI to identify PFO at a high cost and risk of contrast agent allergy. Recent technical advances may have improved the imaging quality and diagnostic accuracy of CCMRI. This is the first study to evaluate the diagnostic value of 3.0T MRI without a contrast agent in detecting PFO.

Our study confirmed that CCMRI could effectively screen for suspected PFO in patients with cerebral disorders and was comparable to cTCD. When combined with pseudo-color coding, CCMRI holds great value for the evaluation and classification of PFO, including its shape, size, blood shunt, and complications such as IAS aneurysm and secondary septum thickening.

The cTCD test in our study found PFO in 88.6% of the patients. It was previously reported that the prevalence of PFO in patients younger than 55 years with cryptogenic stroke was approximately 55% [12]. The difference in prevalence might be due to the examination flow in patients suspected of having PFO in clinical practice. Most patients with a negative cTCD result in this retrospective study were not selected to undergo a CMRI examination, which was associated with a higher prevalence of PFO.

cTEE is currently a widely accepted reference for PFO diagnosis; however, its major drawbacks are invasiveness and considerable dependence on the operator experience. Recent studies have confirmed that cTCD and cTTE, as non-invasive methods, showed a general concordance for PFO diagnosis and could be used for preliminary PFO detections [10]. cTTE is cost-effective and readily available for PFO imaging but has relatively low sensitivity [13], while cTCD is a highly sensitive test and could quantify the severity of RLS. However, it cannot differentiate cardiac from pulmonary shunts or directly visualize the atrial septum [5]. Hence, finding a non-invasive and intuitive modality for PFO diagnosis is crucial for clinical practice.

CMRI is a novel and reliable imaging modality that provides dynamic and objective information on cardiac anatomy. The cine sequence without contrast could be tolerated by most patients. Our study showed that CCMRI had a high sensitivity (94.9%) and concordance (90.9%) for PFO detection compared to cTCD. Two of our cases were found positive for PFO by cTCD, but negative by CCMRI, and were classified as Grade 1 in the cTCD test, indicating that CCMRI might fail in detecting small PFO. Moreover, we highlight that two of our patients were found positive by CCMRI but negative by cTCD, which could correspond to false-negative cases of cTCD. The cause could be an inadequate VM or a higher pressure in the left atrium than the right, resulting in no apparent flow inversion crossing the PFO from right to left.

Mohrs et al. reported that PFO was identified visually in all 15 patients using contrast-enhanced CMRI on a 1.5T scanner, and the sensitivity was 100% when compared with cTEE [7]. In another study with a 1.5T MR system, RLS was detected by contrast-enhanced CMRI in 48 of 72 (66.6%) cases with moderate or severe shunts seen with cTEE, but only in 6 of 32 (18.8%) cases with mild shunts detected by cTEE [8]. Similarly, Hamilton-Craig et al. found that contrast-enhanced CMRI on a 1.5T scanner had a sensitivity of 50%, a specificity of 100%, an NPV of 31%, and a PPV of 100% in detecting PFO when compared to cTEE [9]. In comparison, our study showed that cine sequences without contrast on a 3.0T MR scanner presented an excellent diagnostic value in identifying PFO, indicating that the technical advances of the 3.0T MR scanner improved and optimized the application value of CMRI in PFO detection.

Our study had several limitations. First, the sample size was relatively small, and bias in patient selection in this retrospective study was unavoidable. Second, cTEE was not performed in our cohort. Hence, this study lacked the gold standard for PFO detection. A comparison between cTEE and CCMRI for identifying PFO deserves a prospective evaluation.

In conclusion, CCMRI and pseudo-color coding provided a novel and excellent method for PFO identification, evaluation, and classification in patients with cerebral disorders, with high sensitivity (92.85%) and concordance (90.9%) when compared to cTCD. Dynamic visualization, convenience, and noninvasiveness are important features that allow clinicians to perform a CMRI scan before other modalities when investigating the presence of PFO.

References

1. Lechat P, Mas J L, Lascault G, et al. Prevalence of patent foramen ovale in patients with stroke[J]. N Engl J Med, 1988, 318(18): 1148-52.
2. Powers W J, Rabinstein A A, Ackerson T, et al. 2018 Guidelines for the Early Management of Patients With Acute Ischemic Stroke: A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association[J]. Stroke, 2018, 49(3): e46-e110.
3. Darmoch F, Al-Khadra Y, Bacha H M, et al. Closing the gap on patent foramen ovale and cryptogenic stroke[J]. Expert Rev Cardiovasc Ther, 2019, 17(6): 389-394.

4. Kim Y J, Hur J, Shim C Y, et al. Patent foramen ovale: diagnosis with multidetector CT–comparison with transesophageal echocardiography[J]. Radiology, 2009, 250(1): 61-7.
5. Caputi L, Carriero M R, Falcone C, et al. Transcranial Doppler and transesophageal echocardiography: comparison of both techniques and prospective clinical relevance of transcranial Doppler in patent foramen ovale detection[J]. J Stroke Cerebrovasc Dis, 2009, 18(5): 343-8.
6. Komar M, Olszowska M, Przewłocki T, et al. Transcranial Doppler ultrasonography should it be the first choice for persistent foramen ovale screening?[J]. Cardiovasc Ultrasound, 2014, 12: 16.
7. Mohrs O K, Petersen S E, Erkapic D, et al. Diagnosis of patent foramen ovale using contrast-enhanced dynamic MRI: a pilot study[J]. AJR Am J Roentgenol, 2005, 184(1): 234-40.
8. Nusser T, Höher M, Merkle N, et al. Cardiac magnetic resonance imaging and transesophageal echocardiography in patients with transcatheter closure of patent foramen ovale[J]. J Am Coll Cardiol, 2006, 48(2): 322-9.
9. Hamilton-Craig C, Sestito A, Natale L, et al. Contrast transoesophageal echocardiography remains superior to contrast-enhanced cardiac magnetic resonance imaging for the diagnosis of patent foramen ovale[J]. Eur J Echocardiogr, 2011, 12(3): 222-7.
10. Chen J, Chen L, Hu W, et al. A comparison of contrast transthoracic echocardiography and contrast transcranial Doppler in cryptogenic stroke patients with patent foramen ovale[J]. Brain Behav, 2019, 9(5): e01283.
11. Jauss M, Zanette E. Detection of right-to-left shunt with ultrasound contrast agent and transcranial Doppler sonography[J]. Cerebrovasc Dis, 2000, 10(6): 490-6.
12. Overell J R, Bone I, Lees K R. Interatrial septal abnormalities and stroke: a meta-analysis of case-control studies[J]. Neurology, 2000, 55(8): 1172-9.
13. Mahmoud A N, Elgendy I Y, Agarwal N, et al. Identification and Quantification of Patent Foramen Ovale-Mediated Shunts: Echocardiography and Transcranial Doppler[J]. Interv Cardiol Clin, 2017, 6(4): 495-504.

Tables

Table 1
Baseline characteristics of the study population

Sex (male/female)	**24/20**
Age (mean ± SD years)	41.3 ± 12.1
Migraine headache	16/44 (36.4%)
Visual-field defect	10/44 (22.7%)
Cerebral infarction	7/44 (15.9%)
Transient ischemic attack	5/44 (11.4%)
Convulsion	3/44 (6.8%)
Dizziness	3/44 (6.8%)
SD, standard deviation.	

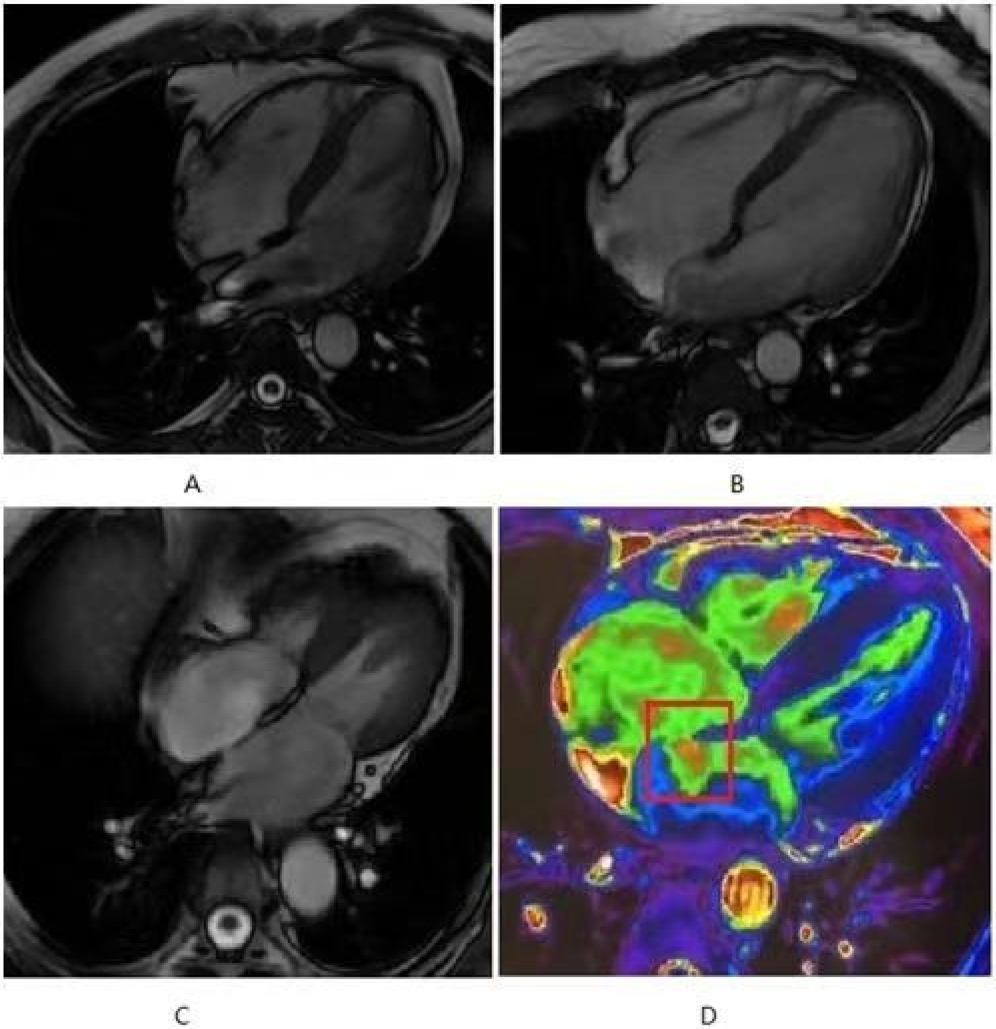
Table 2
cTCD *versus* CCMRI without contrast for PFO detection

	cTCD (-)	**cTCD (+)**	**Total**
CCMRI (-)	3	2	5
CCMRI (+)	2	37	39
Total	5	39	44
cTCD, contrast transcranial Doppler sonography; CCMRI, cardiac cine magnetic resonance imaging; PFO, patent foramen ovale.			

Table 3
CCMRI findings in patients with different RLS grades based on cTCD

	cTCD (+)		
	Grade 1	Grade 2	Grade 3
CCMRI (-)	2	0	0
CCMRI (+)	10	5	22
cTCD, contrast transcranial Doppler sonography; CCMRI, cardiac cine magnetic resonance imaging; RLS, right-to-left shunting.			

Figures



A PFO diagnosed in a 48-year-old male. Cardiac MR image demonstrated the secondary septum thickening of IAS.

B PFO diagnosed in a 37-year-old female. Cardiac MR image revealed the IAS aneurysm.

C PFO diagnosed in a 52-year-old female. Cardiac MR image showed the channel-like appearance of IAS.

D PFO diagnosed in a 29-year-old male. The right-to-left color jet was observed on post-processing images.

Figure 1

PFO was diagnosed in 39 patients by reviewing the CCMRI sequences, of which 37 were positive for RLS in the cTCD test (Table 2). Two of the five patients negative for PFG in CCMRI were positive in the cTCD test, both with Grade 1 RLS (Table 3). Based on post-processing images, the right-to-left color jet was observed in 34 patients, and two-way shunting was found in five. Furthermore, IAS aneurysm and secondary septum thickening were found in five and three patients (11.4 and 6.8%), respectively. Channel-like and latticed appearances of the IAS were detected in six and two patients (13.6 and 4.5%), respectively. The maximum PFO diameters ranged from 1.7 to 16.8 mm, and the mean diameter was 5.4 ± 3.4 mm.