Original Article

Diagnostic Efficacy of Coronary Artery Three-Dimensional Steady-State Free Precession Magnetic Resonance Angiography in Comparison with Invasive Coronary Angiography for Detecting Coronary Artery Disease

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Abstract

Purpose: To assess the diagnostic value of three-dimensional steady-state free precession magnetic resonance angiography (3D-SSFP MRA) for detecting coronary artery disease (CAD).

Materials and Methods: Patients suspected of CAD based on clinical evaluation, underwent invasive coronary angiography (CAG) and Cardiac MRA (CMRA). Collected data in favor of any CAD findings in CMRA were compared to CAG results as the standard diagnostic method in CAD detection. Analysis was performed on per-patient, per-vessel and per-segment bases.

Results: A total of 30 patients (mean age: 43 ± 10 years, 19 men) were enrolled for analysis. On per-patient analysis, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and area under receiver operator characteristic (ROC) curve of CMRA for detection of coronary artery stenosis were 100% (CI95%: 75% – 100%), 50% (CI95%: 18% – 81%), 73.33% (CI95%: 46% – 90%), 100% (CI95%: 47% – 100%) and 0.827, respectively. On per-vessel analysis, CMRA had a sensitivity of 89.29% (CI95%: 71%-97%), specificity of 80.56% (CI95%: 63% – 91%), PPV of 78.13% (CI95%: 60% – 90%), NPV of 90.63% (CI95%: 74% – 98%) and area under ROC curve of 0.845. On per-segment analysis, sensitivity, specificity, PPV and NPV of CMRA for segmental stenosis detection were 77.78% (CI95%: 60% – 89%), 87% (CI95%: 81% – 92%), 62% (CI95%: 46% – 76%), and 93.89% (CI95%: 88% – 97%), respectively. Area under ROC curve was 0.835 on per-segment analysis.

Conclusion: 3D SSFP CMRA provides a promising non-invasive diagnostic tool for assessing coronary artery disease.

Keywords: Coronary angiography, coronary artery disease, magnetic resonance angiography

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Introduction

Cardiovascular disease (CVD) still remains the leading cause of death worldwide, especially throughout the developed countries.[1–3] It is turning into a global epidemic and the most common non-infectious cause of death in Western countries. Regarding the prevalence and the considerable burden imposed on the health care system, it is crucial to curb the complications of CAD through early diagnosis and treatment. Invasive coronary angiography (CAG) is currently the gold standard for CAD detection.[4] Although it allows direct investigation of the coronary artery with high spatial and temporal resolution, it is associated with important drawbacks including its invasiveness, exposure to radiation and use of contrast agents, which can lead to nephrotoxicity and allergic reactions.[2–5] In the past decade, imaging methods, including cardiac magnetic resonance imaging (CMR), have been proposed for diagnosing cardiac pathologies such as CAD, congenital heart diseases (CHD), vascular disorders, and myocardial infarction and its complications. CMR is now considered as one of the best methods for evaluation of cardiac diseases due to its favorable spatial resolution, non-invasiveness, no requirement for technical expertise, no need for contrast agents and consequently low rate of complications.[6] Despite all the advantages, some MRI techniques face pitfalls. Contrast-enhanced magnetic resonance angiography (CE-MRA) has been used for evaluation of thoracic aortic diseases.[5] However, the need for patient's breath-holding cooperation and administration of gadolinium-based contrasts has made it unfeasible in some cases.[5] Steady state free precession (SSFP) MRI sequence allows improved visualization of coronary arteries as it offers higher signal-to-noise ratio (SNR) and contrast-

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to-noise ratio (CNR).[5,7–9] Moreover, the fact that this sequence is free-breathing and its duration depends on patient's breathing pattern makes this sequence more desirable for imaging coronary arteries.[7]

In this study, we intend to evaluate the diagnostic accuracy of 3D free-breathing SSFP CMRA for detection of CAD in comparison to invasive coronary angiography (CAG).

Material and methods

This prospective study was conducted in Rajaie hospital, Tehran, Iran from March 2015 to March 2016. Written informed consent was obtained from all patients prior to enrollment in the study. We enrolled individuals suspected of CAD based on their clinical evaluations who were referred to our center for non-emergent CAG. CAG was performed using Siemens Axiom Artis zee system (Siemens Healthcare Sector, Erlangen, Germany) after administration of 1 to 1.5 mL/kg Iohexol (Omnipaque 300 mg/mL, Little Chalfont, United Kingdom) followed by a 30 mL saline flush. An experienced cardiologist, blinded to clinical conditions of patients, evaluated the results. After 48 hours, the participants underwent CMRA, excluding those with claustrophobia, cardiac pacemaker, any implanted electronic devices, intracranial metal clips, neurostimulators, any metallic object in orbit, hemodynamic instability, tachycardia or dyspnea. All excluded patients received standard care.

All sequences were performed with the patient in supine position, using a 1.5 T, 8-channel body coil Avanto MRI scanner (Siemens Medical, Erlangen, Germany). No contrast injection or breath-holding was required during the study. In order to reduce cardiac motion and respiratory motion artifacts, cardiac-gating and respiratory navigator-gating were used. The space between inferior cardiac border and pulmonary artery was studied as field of view (FOV) in axial, sagittal and coronal views. Respiratory-navigator was placed on the right dome of diaphragm. All 3D SSFP MRA sequences were obtained using the following protocol: Resolution of 256 × 173 mm^2, slice thickness: 1.4 mm, Flip angle: 90°, 50 – 80 slices, bandwidth: 598 HZ/PX, acquisition window 1108. Acquired data were processed on a dedicated workstation using maximum intensity projection (MIP), multi-planar reconstruction (MPR) and volume rendering technique (VRT). Two experienced radiologists, blinded to CAG results, evaluated the extracted images. In case of disagreement, the final diagnosis was made by consensus reading. On CMRA, left anterior descending artery (LAD), right coronary artery (RCA), left circumflex artery (LCX) and left main artery (LM) were investigated. Also, each coronary artery was divided into segments for per-segment analysis (proximal portion, middle portion and distal portion). LAD was subdivided into three segments based on the location of diagonal branches. RCA subdivision into three segments was based on the location of right ventricle branch and RCA bifurcation. LCX was divided into two segments (before and after first obtuse marginal), since its terminal part after second obtuse marginal artery could not be investigated in some of the cases. We also considered LM as a single segment. The images of vessels and segments in some patients did not have the proper quality for assessment. We defined luminal diameter involvement greater than 50% as significant stenosis in our assessments.

The results obtained with CMRA and CAG were compared using SPSS (version 16, IBM Company, USA). Analysis on diagnostic efficacy of CMRA was performed on per-patient, per-vessel and per-segment bases. The diagnostic values for each specific vessel and segment were also calculated. The data was presented as mean ± standard deviation when appropriate. Cross tabulation was used for sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) analysis. Receiver operator characteristic curve (ROC curve) was used to determine the diagnostic accuracy. *P*-value < 0.05 was considered as significant.

Results

Fifty-eight individuals underwent CAG. Twenty-eight patients who did not consent to participation or had a contraindication for MRI were excluded from the study. Finally, a total of 30 individuals underwent CMRI. Figure 1 shows the flowchart of

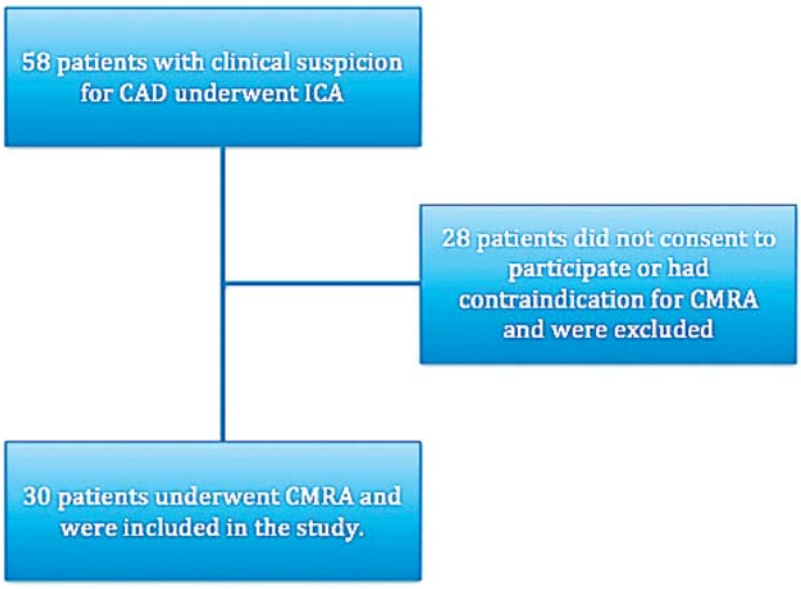

Figure 1. Flowchart of participant selection.

Table 1. CMRA diagnostic values in per–patient, per–vessel and per–segment analyses.

		Sen.(%)[1]	Spec.(%)[2]	PPV (%)[3]	NPV (%)[4]	PLR[5]	NLR[6]	Accur.(%)[7]	Kappa
Per patient (TP = 13, FN = 0, TN = 5, FP = 5)	Estimation	100%	50%	72.2%	100%	2	N/A[81]	78.2%	53%
	95% CI[92]	75%–100%	18%–81%	46%–90%	47%–100%	1.07–3.71	N/A	56%–92%	20%–85%
Per vessel (TP = 25, FN = 3, TN = 57, FP = 7)	Estimation	89.2%	89%	78.1%	95%	8.16	8.31	84.3%	75.3%
	95% CI	71%–97%	78%–95%	60%–90%	86%–98%	4.01–16.61	2.84–24.29	73%–92%	61%–89%
Per segment (TP = 28, FN = 8, TN = 123, FP = 17)	Estimation	77.7%	87.8%	62.2%	93.8%	6.40	3.95	85.8%	60%
	95% CI	60%–89%	81%–92%	46%–76%	88%–97%	3.96–10.33	2.13–7.30	79%–90%	46%–74%

[1]Sensitivity; [2]Specificity; [3]Predictive value of positive test; [4]Predictive value of negative test; [5]Likelihood ratio of positive test; [6]Likelihood ratio of negative test; [7]Diagnostic accuracy; [8]Not applicable; [9]95% Confidence interval.

Table 2. CMRA diagnostic values for each coronary artery.

Diagnostic value	LAD[1]	LCX[2]	RCA[3]
	TP = 13, TN = 6, FP = 4, FN = 0	TP = 6, TN = 13, FP = 2, FN = 0	TP = 6, TN = 9, FP = 2, FN = 3
Sensitivity	100% (CI95: 75%–100%)	100% (CI95%: 54%–100%)	66.6% (CI95%: 29–92%)
Specificity	60% (CI95%: 26%–87%)	86.6% (CI95%: 59%–98%)	81.8% (CI95%: 48%–97%)
PPV	76.4% (CI95%: 50%–93%)	75% (CI95%: 34%–96%)	75% (CI95%: 34%–96%)
NPV	100% (CI95%: 54%–100%)	100% (CI95%: 75%–100%)	75% (CI95%: 42%–94%)
Diagnostic accuracy	82.6% (CI95%: 61%–95%)	90.4% (CI95%: 69%–98%)	75% (CI95%: 50%–91%)
PLR	2.50 (CI95%: 1.17–5.34)	7.50 (CI95%: 2.06–27.25)	3.66 (CI95%: 0.96–13.94)
NLR	N/A	N/A	2.45 (CI95%: 0.93–6.44)
Kappa	62.9% (CI95%: 32%–93%)	78.7% (CI95%: 51%–100%)	48% (CI95%: 10%–87%)

[1]Left anterior descending artery; [2]Left circumflex artery; [3]Right coronary artery

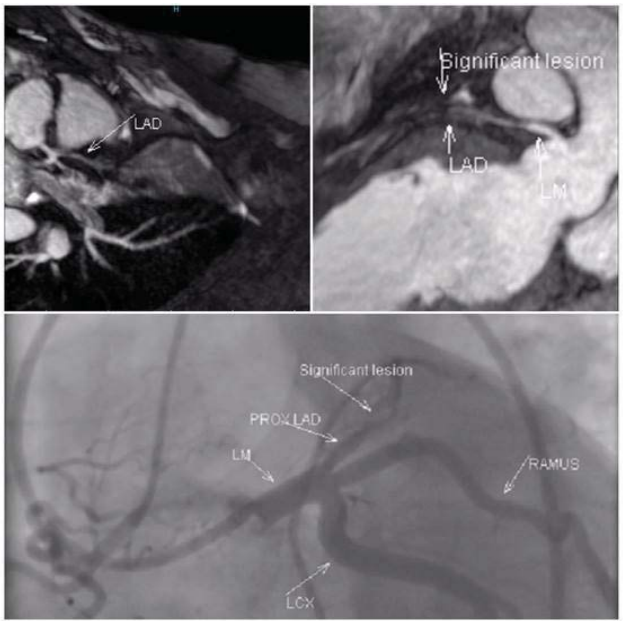

Figure 2. Coronary MRA (top) and corresponding invasive coronary angiography (bottom) in a patient with coronary artery disease. MRA demonstrates a significant stenosis of mid LAD with good correlation with invasive coronary angiography (3 figures)

Table 3. CMRA diagnostic values for each coronary segment in LAD.

Diagnostic value	Proximal segment	Middle segment	Distal segment
	TP = 1, TN = 12, FP = 0, FN = 2	TP = 5, TN = 11, FP = 4, FN = 0	TP = 2, TN = 13, FP = 2, FN = 0
Sensitivity	33.3% (CI95: 0%–90%)	100% (CI95: 47%–100%)	100% (CI95%:15%–100%)
Specificity	100% (CI95%: 73%–100%)	73.3% (CI95%: 44%–92%)	86.6% (CI95%: 59%–98%)
PPV	100% (CI95%: 2%–100%)	55.5% (CI95%: 21%–86%)	50% (CI95%: 6%–93%)
NPV	85.7% (CI95%: 57%–98%)	100% (CI95%: 71%–100%)	100% (CI95%: 75%–100%)
Diagnostic accuracy	86.6% (CI95%: 59%–98%)	80% (CI95%: 56%–94%)	88.2% (CI95%: 63%–98%)
PLR	N/A	3.75 (CI95%: 1.62–8.67)	7.50 (CI95%: 2.06–27.25)
NLR	1.5 (CI95%: 0.67–3.33)	N/A	N/A
Kappa	44.4% (CI95%: 0%–100%)	57.8% (CI95%: 24%–91%)	60.4% (CI95%: 13%–100%)

including participants. The mean age of enrolled patients was 43 ± 10 years and 19 (63.3%) of them were men. Significant stenosis of coronary arteries was found in 18 (60%) patients based on CAG investigations.

Per-patient analysis for stenosis detection

Area under ROC curve for CMRA in comparison to CAG was 0.827. Table 1 presents the sensitivity, specificity, PPV, NPV, likelihood ratio of positive test (PLR), likelihood of negative test (NLR), diagnostic accuracy and kappa index of CMRA for detection of coronary artery stenosis.

Per-vessel analysis for stenosis detection

Area under Roc curve for CMRA in comparison to CAG was 0.845. Table 1 presents the sensitivity, specificity, PPV, NPV, PLR, NLR, diagnostic accuracy and kappa index of CMRA for detection of coronary artery stenosis. Table 2 outlines the CMRA diagnostic values for coronary stenosis detection in each coronary artery. Since ICA and CMRA investigations did not find any stenosis in LM artery in our patients, specific diagnostic values for LM artery could not be calculated.

Per-segment analysis for stenosis detection

Area under ROC curve for CMRA in comparison to CAG was 0.835. Table 1 presents the sensitivity, specificity, PPV, NPV, PLR, NLR, diagnostic accuracy and kappa index of CMRA for detection of segmental stenosis. Tables 3 – 5 show the diagnostic values of CMRA for coronary stenosis detection in each coronary segment.

Discussion

In the present study, we intended to determine the diagnostic efficacy of 3D SSFP whole-heart CMRA in comparison to CAG for detecting CAD. Invasive procedures such as CAG still remain the gold standard for CAD evaluation. In comparison to CMRA, these methods are associated with certain drawbacks, especially complications due to using contrast agents. However, unlike

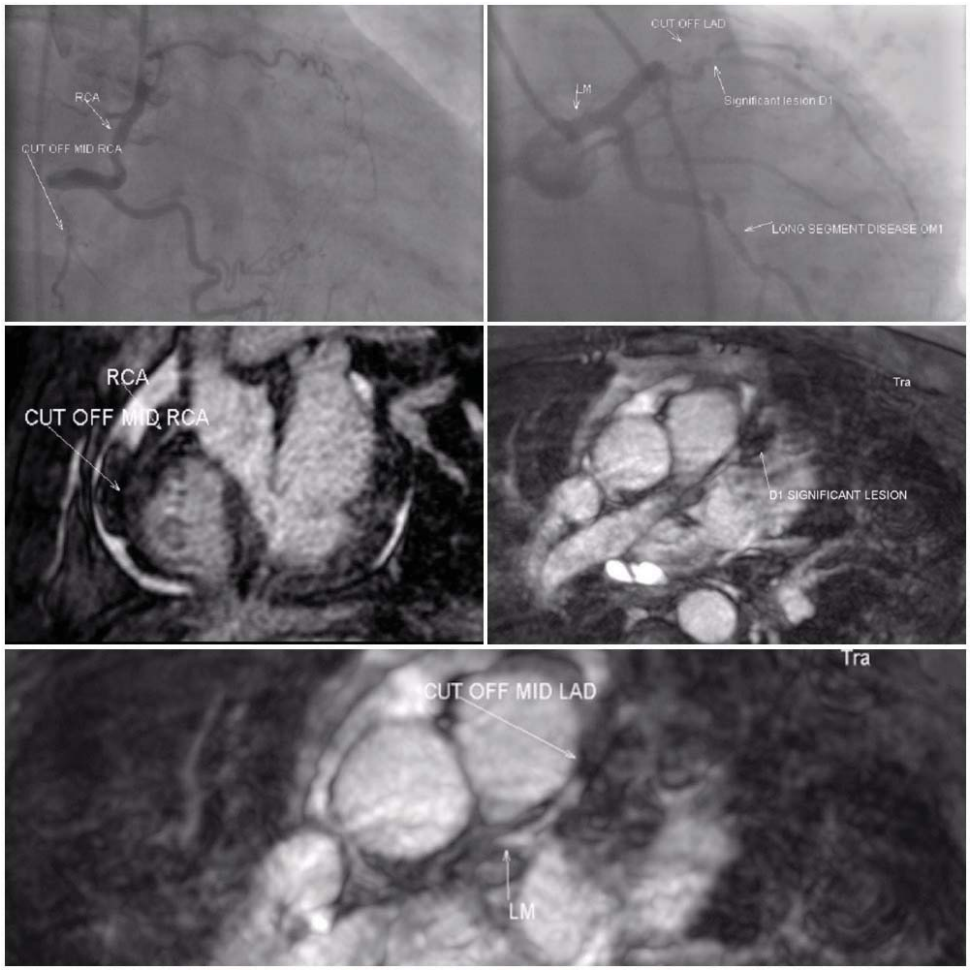

Figure 3. A significant stenosis of D1 and cut-off of mid LAD and mid portion of RCA in another patient is depicted in MRA and corresponds well with invasive coronary angiography .

Table 4. CMRA diagnostic values for each coronary segment in RCA.

Diagnostic value	Proximal segment	Middle segment	Distal segment
	TP = 5, TN = 12, FP = 2, FN = 1	TP = 1, TN = 10, FP = 1, FN = 3	TP = 1, TN = 12, FP = 0, FN = 2
Sensitivity	83.3% (CI95: 35%–99%)	25% (CI95: 0%–80%)	33.3% (CI95%: 0%–90%)
Specificity	85.7% (CI95%: 57%–98%)	90% (CI95%: 58%–99%)	100% (CI95%: 73%–100%)
PPV	71.4% (CI95%: 29%–96%)	50% (CI95%: 1%–98%)	100% (CI95%: 2%–100%)
NPV	92.3% (CI95%: 63%–99%)	76.9% (CI95%: 46%–94%)	85.7% (CI95%: 57%–98%)
Diagnostic accuracy	85% (CI95%: 62%–96%)	73.3% (CI95%: 44%–92%)	86.6% (CI95%: 59%–98%)
PLR	5.83 (CI95%: 1.5–22.1)	2.75 (CI95%: 0.22–34.33)	N/A
NLR	5.14 (CI95%: 0.8–31.1)	1.21 (CI95%: 0.66–2.19)	1.50 (CI95%: 0.67–3.33)
Kappa	65.9% (CI95%: 30%–100%)	18% (CI95%: 0%–70%)	44.4% (CI95%: 0%–100%)

Table 5. CMRA diagnostic values for each coronary segment in LCX.

Diagnostic value	Proximal	Distal
	TP = 3, TN = 15, FP = 3, FN = 0	TP = 2, TN = 11, FP = 1, FN = 1
Sensitivity	100% (CI95: 29%–100%)	66.6% (CI95: 9%–99%)
Specificity	83.3% (CI95%: 58–96%)	91.6% (CI95%: 61%–99%)
PPV	50% (CI95%: 11%–88%)	66.6% (CI95%: 9%–99%)
NPV	100% (CI95%: 78%–100%)	100% (CI95%: 54%–100%)
Diagnostic accuracy	85.7% (CI95%: 63%–96%)	91.6% (CI95%: 61%–99%)
PLR	6 (CI95%: 2.1–16.8)	8 (CI95%: 1.04–61.5)
NLR	N/A	2.75 (CI95%: 0.55–13.7)
Kappa	58.8% (CI95%: 19%–98%)	58.3% (CI95%: 6%–100%)

CAG, CMRA can only distinguish significant stenosis (> 50%) from insignificant stenosis (< 50%) without providing further information on grading of stenosis.

CMRA also offers some benefits in comparison to other non-invasive diagnostic methods such as multi detector computed tomography (MDCT). Although MDCT has high diagnostic accuracy, it is associated with certain drawbacks.[4] Exposure to radiation, dependence on patient's heart rate variations and beam hardening artifacts due to artery calcification have made the use of MDCT for detection of CAD challenging.[4,10] CMRA offers some advantages over MDCT regarding exposure to radiation and its capability to overcome motion artifacts. Despite the benefits of coronary MR angiography, it has major limitations in comparison with CT-angiography (CTA) including operator dependency, lower spatial resolution and long acquisition time. The mean acquisition time of CMRA in our study was 3.5 – 5 minutes.

We demonstrated that whole heart CMRA has high sensitivity (100%), intermediate specificity (50%), fairly acceptable PPV (72.2%) and high NPV (100%). This rate of NPV shows that CMRA can reliably rule out CAD in suspected low-risk patients. Several studies have evaluated the diagnostic efficacy of CMRA for CAD detection and yielded different outcomes. Our results compare favorably with other studies on this matter. Greenwood, et al. demonstrated that CMR had 86.5% sensitivity, 83.4% specificity, 77.2% PPV and 90.5% NPV in comparison to CAG.[11] In a study conducted by Kwong, et al. CMR had 84% sensitivity and 85% specificity for diagnosing acute coronary syndrome.[12] Josefson, et al. showed that CMR had 82% sensitivity for diagnosis of stenosis in one vessel and 88% for detecting pathology in two arteries.[13] De Mello-RA, et al. reported a sensitivity of 65% for CMR for CAD diagnosis.[14] In a study performed on 138 subjects by Kato, et al. using a 1.5T 3D navigator-gated SSFP whole-heart CMRA, it 88% sensitivity, 72% specificity, 71% PPV, 88% NPV and 79% diagnostic accuracy were found for diagnosis of significant coronary stenosis.[15] Regarding the diagnostic values of CMRA, it can be concluded that negative CMRA results can almost exclude CAD, whereas positive results may warrant further investigations. As a matter of fact, the main application of CMRA is to exclude CAD; in case of normal results, further investigation would be unnecessary with conventional angiography or computed tomography angiography (CT angiography). Besides, CMRA can be a promising alternative diagnostic method in individuals for whom angiography is considered as high-risk such as patients with renal insufficiency, hemodynamic instability or cardiomyopathy. We also demonstrated that 3D SSFP whole-heart CMRA can promisingly detect significant stenosis in involved vessels and even arterial segments. Nevertheless, there are some downsides associated with using CMRA such as the fact that some arterial segments (mostly distal segment of LCX in our study) could not be evaluated due to low quality of acquired images. Some patient-related conditions can also limit the use of CMRA, such as severe obesity, claustrophobia or any implanted electronic devices.

Our study had some limitations. A larger sample size would yield more reliable outcomes. Furthermore, some obtained images did not have the proper quality for analysis. Some arterial segments could not be evaluated by CMRA, either. In our study, LCX was subdivided into two segments, as we could not evaluate the arterial segment after second obtuse marginal artery. Hence, larger studies with technical improvements are needed to evaluate distal segments and corroborate our findings.

In conclusion, according to the results of this study, 3D SSFP CMRA is an efficient method for assessment of cardiovascular diseases and could be used as a promising alternative to invasive coronary angiography, considering the fact that fewer complications are associated with CMRA in comparison to CAG.

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Conflict of interests: *None declared.*

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