The International Journal of Cardiovascular Imaging (2019) 35:897–905
https://doi.org/10.1007/s10554-019-01531-x

ORIGINAL PAPER

Assessment of coronary flow velocity reserve with phase-contrast cine magnetic resonance imaging in patients with heavy coronary calcification

Takatoshi Higashikawa[1] · Yasutaka Ichikawa[1] · Masaki Ishida[1] · Kakuya Kitagawa[1] · Tadanori Hirano[2] · Hajime Sakuma[1]

Received: 4 November 2018 / Accepted: 7 January 2019 / Published online: 25 February 2019

Abstract

Coronary flow velocity reserve (CFVR) can be noninvasively measured by phase-contrast cine magnetic resonance imaging (PC-MRI). Heavy coronary calcification degrades the diagnostic accuracy for the detection of coronary arterial stenosis on computed tomography (CT). The aim of this study was to evaluate the value of CFVR measurement with PC-MRI for detecting significant coronary stenoses in patients with heavy coronary calcification. Sixteen patients (71 ± 8 years) with coronary calcium score above 400 who had suspected moderate coronary stenosis (50–69% diameter stenosis) on CT angiography were prospectively studied. The CFVR values, calculated as the ratio of peak flow velocity during hyperemia to the peak flow velocity at rest, were measured using breath-hold PC-MRI with 3 T system, and were compared with the results of quantitative coronary angiography (QCA). The mean coronary calcium score was 985 ± 378. CFVR was successfully determined with PC-MRI in 17/18 (94%) vessels. Using a threshold of 1.4 for CFVR, the sensitivity, specificity, and positive and negative predictive value for detecting ≥ 50% stenosis on QCA was 88% (7/8), 89% (8/9), 88% (7/8), 89% (8/9), respectively. When MRI CFVR measurements was added to CT angiography for the evaluation of coronary stenosis, the positive predictive value was 88% (7/8), while the positive predictive value of CT angiography alone was 44% (8/18). PC-MRI can provide noninvasive detection of altered CFVR caused by significant stenosis in patient. CFVR measurement by PC-MRI is useful for diagnosing physiologically significant coronary stenosis in patients with high calcium score on CT.

Keywords Magnetic resonance imaging · Coronary vessels · Coronary stenosis · Coronary flow velocity reserve

✉ Takatoshi Higashikawa
higashikawat@clin.medic.mie-u.ac.jp

Yasutaka Ichikawa
yasutaka@clin.medic.mie-u.ac.jp

Masaki Ishida
mishida@clin.medic.mie-u.ac.jp

Kakuya Kitagawa
kakuya@clin.medic.mie-u.ac.jp

Tadanori Hirano
t-hirano@clin.medic.mie-u.ac.jp

Hajime Sakuma
sakuma.mie@gmail.com

[1] Department of Radiology, Mie University Hospital, 2-174 Edobashi, Tsu, Mie 514-8507, Japan

[2] Department of Radiology, Matsusaka Central Hospital, 102 Kobou, Kawai, Matsusaka, Mie 515-8566, Japan

Introduction

Phase-contrast cine magnetic resonance imaging (PC-MRI) is a noninvasive method to quantify blood volume flow and velocity. Shibata et al. demonstrated that flow quantification in the coronary artery with PC-MRI is feasible and coronary flow velocity reserve (CFVR) determined by PC-MRI is significantly correlated with that by intracoronary Doppler echo technique [1]. CFVR assessment with PC-MRI has a potential to detect in-stent restenosis in the coronary arteries [2, 3]. PC-MRI may allow for noninvasive quantitative assessment of functional significance of coronary arterial stenosis.

Coronary computed tomography (CT) angiography has proven to be useful for noninvasive detection of coronary arterial stenosis. However, heavy coronary calcification degrades the diagnostic accuracy, especially in specificity, for detecting obstructive coronary artery disease by CT angiography. In a previous meta-analysis, the specificity of

CT angiography for the detection of significant coronary stenosis was 42% (28–56%) in patients with coronary calcium score above 400 [4]. Arbab-Zadeh et al. reported that CT angiography is less effective in patient with coronary calcium score above 600 [5].

Since flow measurement with PC-MRI is hardly affected by calcification, PC-MRI might be useful to assess coronary arterial stenosis in patients with heavy coronary calcification. We conducted this study to evaluate the usefulness of CFVR measurement with PC-MRI for detecting coronary arterial stenosis in a cohort of patients with severe coronary arterial calcification detected on CT.

Materials and methods

Patients

Patients who underwent coronary CT examinations for suspected ischemic heart disease, had coronary calcium score of > 400 [6], suspected of having moderate coronary stenosis (50–70% diameter stenosis) with reference diameter of > 2.5 mm on CT angiography performed between May and December 2013, and scheduled invasive coronary angiography, were prospectively recruited to undergo the coronary flow measurement with PC-MRI. Patient who had myocardial infarction, unstable angina, previous coronary artery bypass grafting, irregular heart rhythm (arterial fibrillation, frequent premature arterial complexes, etc.), pacemaker, claustrophobia, or contraindication to receiving adenosine triphosphate were excluded from this study. All patients provided informed consent to participate in this study, which was approved by the local institutional review board. Coronary CT examinations, comprising pre-contrast CT for coronary calcium scoring and coronary CT angiography, were obtained with 64-slice CT (Lightspeed VCT, GE Healthcare, Milwaukee, WI). Pre-contrast CT was performed with a retrospective electrocardiographic-gated helical scan with low-tube current (150 mA), gantry rotation time of 350 ms, pitch of 0.18, tube voltageof 120 kV, and scan field of view of 250 mm. For post-contrast cardiac CT, 65 to 85 mL of iohexol (350 mg/mL) was into the antecubital vein at an injection speed of 4 mL/s, followed by a 20-mL saline bolus (injection rate, 4 mL/s). Post-contrast cardiac CT was obtained with retrospective gating and scan parameters as follows: gantry rotation time, 350 ms; pitch, 0.24; tube voltage, 120 kV; tube current 680 to 750 mA; scanning field of view, 180 mm. Oral-beta blocker medication was given if the heart rate was > 65 beats/min (metoprolol, 20–60 mg, one hour before examination). Isosorbide dinitrate (5 mg) was sublingually administered before CT acquisition in all subjects. Coronary calcium scoring was performed using the Agatston scoring method which has been previously descried[6]. Two experienced radiologists evaluated the presence or absence, and stenotic severity in the coronary arteries on CT angiography by consensus, based on Coronary Artery Disease Reporting and Data System (CAD-RADS) [7].

Acquisition of MR data

MR images were acquired on a 3 T (T) scanner (Ingenia, Philips Healthcare, Best, Netherlands). Subjects were asked to abstain from caffeine-containing products for at least 12 h prior to the magnetic resonance examinations. Following scout imaging, high temporal resolution transaxial cine MR images were firstly acquired with a steady-state free precession sequence during a single breath holding at shallow expiration (cardiac phases of 50, repetition time of 2.6 ms, echo time of 1.3 ms, flip angle of 45 degree, field of view of 350 × 350 mm, SENSE factor of 3, acquisition matrix of 128 × 128, reconstruction matrix of 256 × 256, slice thickness of 8 mm) to determine the rest period of the right coronary artery during the diastolic phase. Then, 3-dimensional respiratory-gated whole heart coronary MR angiography were performed to determine the imaging plane for PC-MRI. The coronary MR angiography was obtained with a fast field echo sequence with radial k-space sampling, repetition time of 3.6 ms, echo time of 1.7 ms, flip angle of 15 degree, field of view of 330 × 280 mm, SENSE factor of 2.2, acquisition matrix of 256 × 256, reconstruction matrix of 512 × 512, slice thickness of 1.5 mm, T2 preparation, and spectral presaturation with inversion recovery. The coronary MR angiography was used to determine the site of coronary arteries for flow measurement. The MR flow measurement was aimed at the site distal to the coronary arterial stenosis suspected on CT angiography. In order to determine the site of MR flow measurement, firstly, the coronary stenotic site was identified on MR angiography by referring the coronary CT angiography. Then, the coronary site for flow measurement was determined so as to be approximated to the respective coronary stenotic site as much as possible on MR angiography. Multiplanar reformation of whole heart coronary MR angiography was used to determine double oblique imaging plane that is perpendicular to the coronary artery (Fig. 1). PC-MRI was acquired on the imaging plane that was perpendicular to the coronary artery at rest and during hyperemia status induced by adenosine triphosphate (160 μg/kg/min). PC-MRI was performed during a single breath holding at shallow expiration, with a section thickness of 6 mm, a repetition time of 5.0 ms and an echo time of 3.2 ms, a field of view of 180 × 156 mm, phase per cardiac cycle of 25, an acquisition matrix of 192 × 168, acquisition pixel size of 1.2 × 1.9 mm, and reconstructed pixel size of 0.9 × 0.9 mm. Velocity encoding gradients were applied in the slice-selective direction with velocity window of ± 80 cm/s at rest and

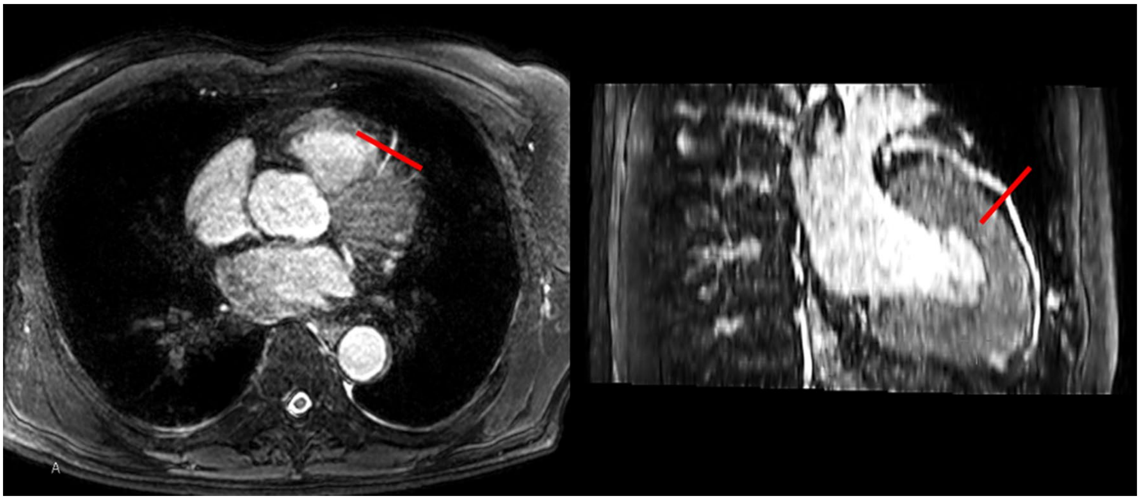

Fig. 1 Multiplanar reformation of whole heart coronary MR angiography was used to determine double oblique imaging plane that is perpendicular to the target vessel. PC-MRI was obtained at a site distal to the stenosis

± 120 cm/s during vasodilator stress because peak velocity in the coronary artery can exceed 80 cm/sec after pharmacologic stress according to a previous study [8].

Image analysis of coronary PC-MRI

Assessing flow velocity with PC-MRI was performed in random order by a dedicated software (CVi 42; Circle Cardiovascular Imaging Inc, Calgary, Canada). Coronary arteries were manually traced on the magnitude images and the regions of interest (ROI) were automatically reflected on the phase difference images. The flow velocity (cm/s) in the ROI was measured on each magnitude image throughout cardiac cycle by two independent observers blinded to clinical information of the subjects. The highest value was used for the determination of peak coronary flow velocity. To compensate for the through-plane motion and phase offset error, a second ROI was placed on adjacent adipose tissue and the velocity of the adjacent tissue through plane motion was determined and subtracted from the intracoronary flow values [1]. CFVR was calculated as the ratio of the peak flow velocity during hyperemia to the peak flow velocity at rest. The CFVR measurement was performed by two radiologists, independently.

X-ray coronary angiography

In all subjects, selective coronary angiography were performed on the next day of the PC-MRI examinations. Quantitative assessment was performed using quantitative coronary angiography (QCA) (QAngioXA7.1, Medis medical imaging system, The Netherlands) by an experienced observer. The coronary arteries were divided into two lesion groups based on the results of QCA (non-stenotic vessel group, < 50% diameter stenosis on QCA; stenotic vessel group, ≥ 50% diameter lesion stenosis on QCA) for the analysis.

Statistical analysis

Continuous values are described as means and standard deviation. Differences in coronary peak flow velocity and CFVR between the non-stenotic coronary lesions and the stenotic lesions on QCA were analyzed by Mann–Whitney U test. Differences in peak flow velocity between at rest and during vasodilator stress were analyzed by Wilcoxon matched-pairs signed rank test. Comparison between results from QCA and PC-MRI was performed using a linear regression analysis. Inter- -observer reproducibility were analyzed with the intraclass correlation coefficient (ICC). The ICC was derived as a measurement of agreement between observers. The ICC of > 0.9, 0.75–0.9 and 0.4–0.75 was defined as excellent, good and fair agreement, respectively. A two-sided p value of < 0.05 was considered to indicate statistical significance. All statistical analyses were performed with SPSS software, version 17.0 (SPSS, Inc., Chicago, IL, USA).

Results

Of 256 patients who underwent coronary CT angiography performed between May and December 2013 at the institute, 12 patients were excluded from this study because of coronary artery bypass grafting, 13 were excluded by a history of myocardial infarction, 5 were excluded by irregular heart rhythm and one patient was excluded by pacemaker replacement. Eventually, 16 patients (11 men and 5 women; mean age, 71 ± 8 years; mean coronary calcium score, 985 ± 378) met the inclusion criteria and were recruited to this study. Patient characteristics are listed in Table 1. The mean interval between the coronary CT and the PC-MRI examinations was 39 ± 22 days, ranging from 13 to 89 days. No significant medical event was documented during the intervals between CT and PC-MRI examinations. Eighteen coronary arteries, including 5 right coronary artery (RCA), 11 left anterior descending (LAD) artery, and 2 left circumflex (LCX) artery, were evaluated by PC-MRI. The details of the coronary segments in which PC-MRI assessment was performed in this study are shown in Table 2. The mean distance between the stenotic sites and the flow measurement sites was 34 ± 19 mm. CFVR values were successfully determined in 17/18 (94%) vessels. Representative cases are presented in Figs. 2, 3 and 4. In one LAD artery in a subject, the determination of CFVR with PC-MRI was failed, since the LAD artery was extremely tortuous and we could not determine the adequate imaging plane perpendicular to the coronary artery.

Coronary stenoses with 50% or greater on QCA were detected 8 of 18 (44%) vessels. The mean CFVR in the coronary artery with < 50% stenosis on QCA was significantly higher than that with ≥ 50% stenosis on QCA (1.9 ± 0.4 vs. 1.3 ± 0.4, p = 0.0055) (Table 3). The peak flow velocity during vasodilator stress was significantly higher than that at rest (17.6 ± 5.0 cm/s vs. 9.6 ± 2.9 cm/s, p = 0.0039) in the coronary arteries with < 50% stenosis, while the peak flow

Table 1 Patient characteristics

Total number of patient, n	16
Men, n (%)	11 (69)
Women, n (%)	5 (31)
Age(years)	71 ± 8
Heart rate(beats/min)	65.7 ± 15.7
Body mass index (kg/m^2)	23.9 ± 4.1
Clinical diagnosis	
Smoking, n (%)	5 (31)
Hypertension, n (%)	12 (75)
Hypercholesterinemia, n (%)	12 (75)
Diabetes mellitus, n (%)	9 (56)
Medication	
Aspirin, n (%)	11 (69)
Statin, n (%)	11 (69)
β-blocker, n (%)	4 (25)
Nitrate, n (%)	1 (6)
ACE inhibitor, n (%)	9 (56)
Calcium antagonist, n (%)	6 (38)
Coronary calcium score	986 ± 366

Table 2 Summary of the measurements of QCA and coronary PC-MRI

coronary artery No.	Coronary segment suspected of having moderate stenosis on CT	QCA measurements (%)	Reference diameter on QCA (mm)	Coronary segment assessed by PC-MRI	Peak flow velocity at rest (cm/s)	Peak flow velocity during vasodilator stress (cm/s)	CFVR
1	#4AV	69.6	2.6	#4AV	8.9	10.3	1.2
2	#11	52.5	1.8	#11	12.1	27.5	2.3
3	#7	39	2.0	#7	12.4	18.8	1.5
4	#7	74.9	2.2	#7	6.2	8.3	1.4
5	#6	66.4	3.5	#7	11.2	14.0	1.3
6	#4AV	73.2	2.9	#4AV	6.0	6.0	1
7	#8	59.1	2.0	#8	5.7	7.1	1.2
8	#7	31.8	3.0	#8	15.3	25.9	1.7
9	#7	n/a	n/a	#8	n/a[a]	n/a[a]	n/a[a]
10	#6	32.3	2.7	#7	8.8	21.4	2.4
11	#3	48.6	2.8	#3	6.5	15.4	2.4
12	#7	47.3	2.3	#7	9.3	20.4	2.2
13	#11	29.7	2.8	#11	7.4	13.3	1.8
14	#7	43	2.4	#8	10.5	14.2	1.4
15	#3	24	2.9	#3	9.9	19.7	2.0
16	#2	59.4	2.7	#4	7.7	7.0	0.9
17	#7	51.3	3.3	#8	7.5	8.7	1.2
18	#6	30.6	2.6	#7	6.4	9.4	1.5

CTA computed tomography, *QCA* quantitative coronary angiography, *PC-MRI* phase-contrast cine magnetic resonance imaging, *CFVR* coronary flow velocity reserve

[a]The acquisition of PC-MRI was failed

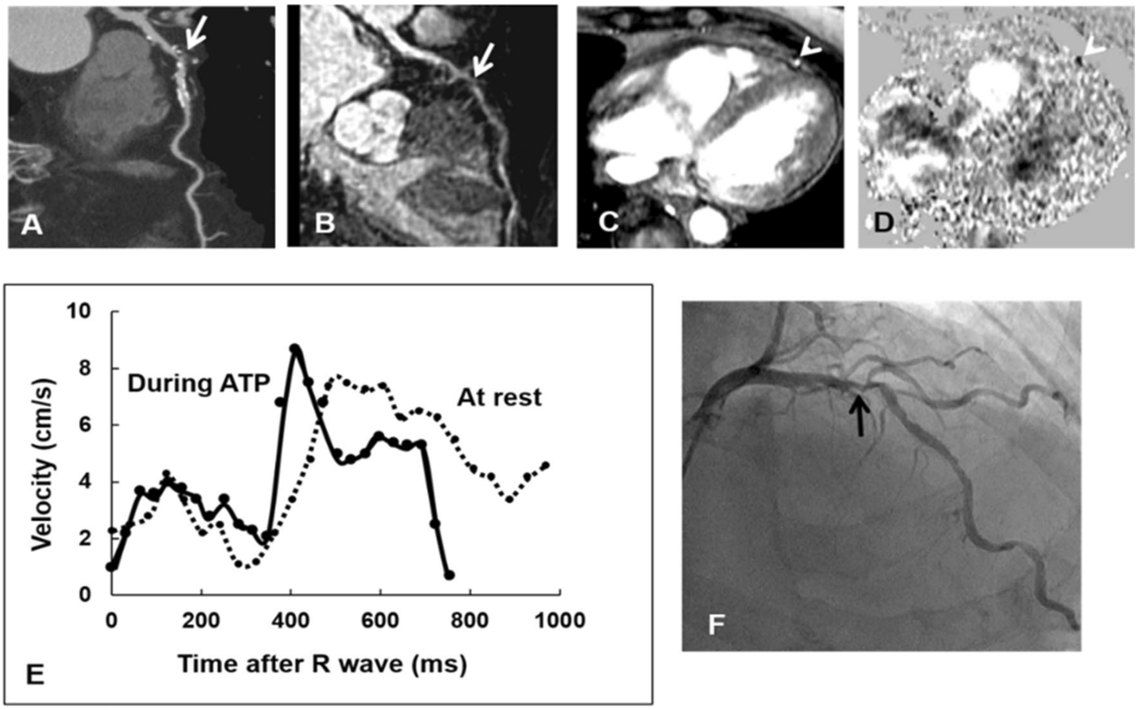

Fig. 2 (vessel case 17) In a 77-year old man with Agaston score of 1549, moderate stenosis was suspected in the proximal LAD artery on CT angiography (**a**, arrow). MR angiography shows stenosis at the corresponding site of LAD artery (**b**, arrow). Magnitude image (**c**) and phase difference image (**d**) of the LAD artery distal to the stenosis are presented. **e** Time-velocity curves at rest and during vasodilator stress in this patient are determined. Peak flow velocity was 7.5 cm/sec at rest and 8.7 during hyperemia, indicating CFVR of 1.2. On X-ray coronary angiography, moderate to severe stenosis was detected in the LAD artery (diameter stenosis on QCA, 51%) (F, arrow)

velocity during stress was not statistically different from that at rest (11.0 ± 7.1 cm/s vs. 8.4 ± 2.4 cm/s, p = 0.56) in the coronary arteries with ≥ 50% stenosis on QCA. The peak timing of coronary flow velocity was observed at diastolic phase for both rest and stress in the all coronary arteries examined.

The correlation between luminal narrowing determined by QCA and CFVR by MRI is shown in Fig. 5. Significant moderate inverse correlation was found between the percent luminal stenosis determined by QCA and the CFVR determined by PC-MRI (r = − 0.53). The area under receiver operating characteristics (ROC) curve was 0.89 for CFVR in the detection of luminal narrowing of ≥ 50% by invasive angiography. With a threshold value of 1.4 that was determined by ROC analysis, the sensitivity, specificity, and positive and negative predictive value for detecting ≥ 50% stenosis on QCA was 88% (7/8), 89% (8/9), 88% (7/8), 89% (8/9), respectively. Intra-class correlation coefficient between CFVR measurements by two observers was 0.82.

The positive predictive value of CT angiography for detecting ≥ 50% stenosis on QCA was 44% (8/18) in vessel-base. False positive was found in 10 vessels (56%, 10/18) on CT angiography alone. When MRI CFVR measurements was added to CT angiography for the evaluation of coronary stenosis, the positive predictive value of CT angiography for detecting ≥ 50% stenosis on QCA was improved to 88% (7/8) and the false positive was decreased to 1 vessel.

Discussion

The current study demonstrated that PC-MRI can provide noninvasive detection of altered CFVR caused by significant stenosis in patients with severe coronary calcification. CFVR measurement by PC-MRI has a potential to rule out physiologically significant coronary stenosis in patients who have high calcium score and suspected coronary artery disease on CT angiography.

It is known that CFVR is an excellent marker of the functional significance of coronary arterial stenosis [9], and abnormal CFVR is associated with adverse clinical outcomes [10]. Accordingly, CFVR can provide important implications for the clinical management in patients with coronary arterial disease. Doppler guide wire has been used for evaluating coronary blood flow and blood velocity [11–13]. However, the assessment with Doppler guide wire is invasive method and has potential risks and complications. To date, transthoracic Doppler echocardiography

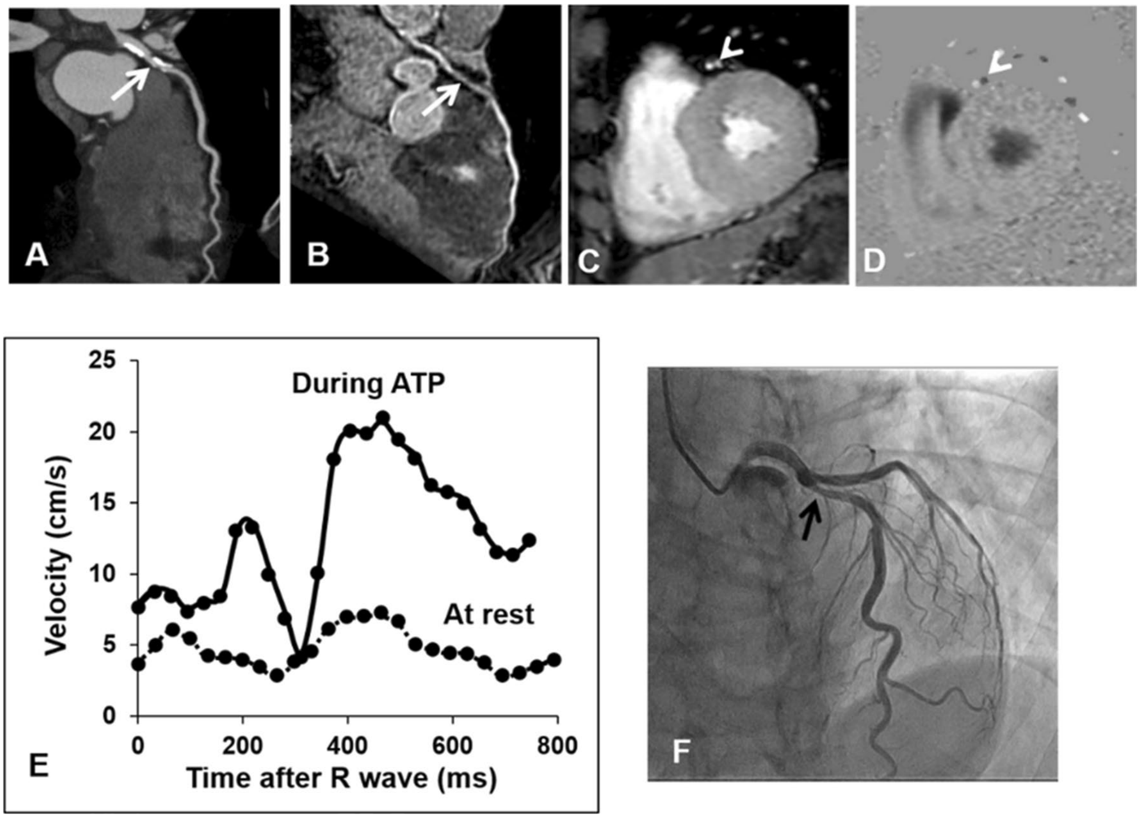

Fig. 3 (vessel case 10) In a 75-year old man with Agaston score of 1177, moderate stenosis was suspected in the proximal LAD on CT angiography and MR angiography (**a, b**). Magnitude image (**c**) and phase contrast image (**d**) of the LAD artery distal to the lesion. **e** Peak flow velocity was 8.8 cm/sec at rest and 21.4 during hyperemia, indicating CFVR of 2.4. On coronary angiography, mild stenosis was depicted at the proximal LAD artery (diameter stenosis on QCA, 32%) (**f**)

and PC-MRI have been reported as noninvasive methods of choice for evaluating CFVR [1–3, 14, 15]. Previous studies demonstrated that the CFVR assessment by Doppler echocardiography is useful for detecting flow-limiting stenosis in LAD artery [14, 15]. However, Doppler echocardiography is of limited use in RCA and LCX artery. PC-MRI has potential to evaluate coronary stenosis not only in LAD artery but also RCA and LCX artery [2, 3].

Blood flow measurements with PC-MRI in large vessels, such as the aorta, pulmonary and carotid artery, have been well validated [16–18]. PC-MRI has also been applied to the smaller vessels such as coronary sinus [19–21] and coronary artery bypass graft [22] for the flow quantification. Previous studies demonstrated the feasibility of coronary arterial flow quantification with PC-MRI [1–3]. Shibata et al. reported that the CFVR determined by PC-MRI in the LAD arteries in 19 patients was 2.00 ± 0.87, showing no significant differences with that determined by Doppler guide wire (2.41 ± 1.38) [1]. Hundley et al. reported that PC-MRI CFVR value ≤ 2.0 was 100% and 82% sensitive and 89% and 100% specific for detecting a luminal diameter narrowing of $\geq 75\%$ and 50%, respectively [2]. Another study reported that regression analysis for CFVR determined with PC-MRI and Doppler resulted in a slope of 1.04 ($r = 0.89$) in 29 patients with coronary artery diseases [3]. They reported that, with a threshold value of 1.2 of PC-MRI CFVR, the sensitivity, specificity, and positive and negative predictive value for detecting $\geq 50\%$ in-stent restenosis on QCA was 85%, 89%, 94%, and 73%, respectively [3]. To date, CEVR assessment with PC-MRI has been generally of limited use in the LAD artery. The current study included RCA and LCX artery as well as LAD artery for the CFVR measurement.

To date, 1.5 T (T) system has been used for the study of coronary arterial flow quantification with PC-MRI. Recently, 3T system is available for the cardiac MR study in many institutions. When compared with 1.5T MR system, 3T system can provide better signal-to-noise ratio on PC-MRI. Higher signal-to-noise ratio might be useful for reliable flow quantification with PC-MRI in small vessels such as coronary arteries. To our knowledge, this study is the first to apply 3T system for the CFVR assessment in patients who were suspected coronary artery disease.

In patients with high coronary artery calcium score, calcified plaques may obscure luminal changes and can often

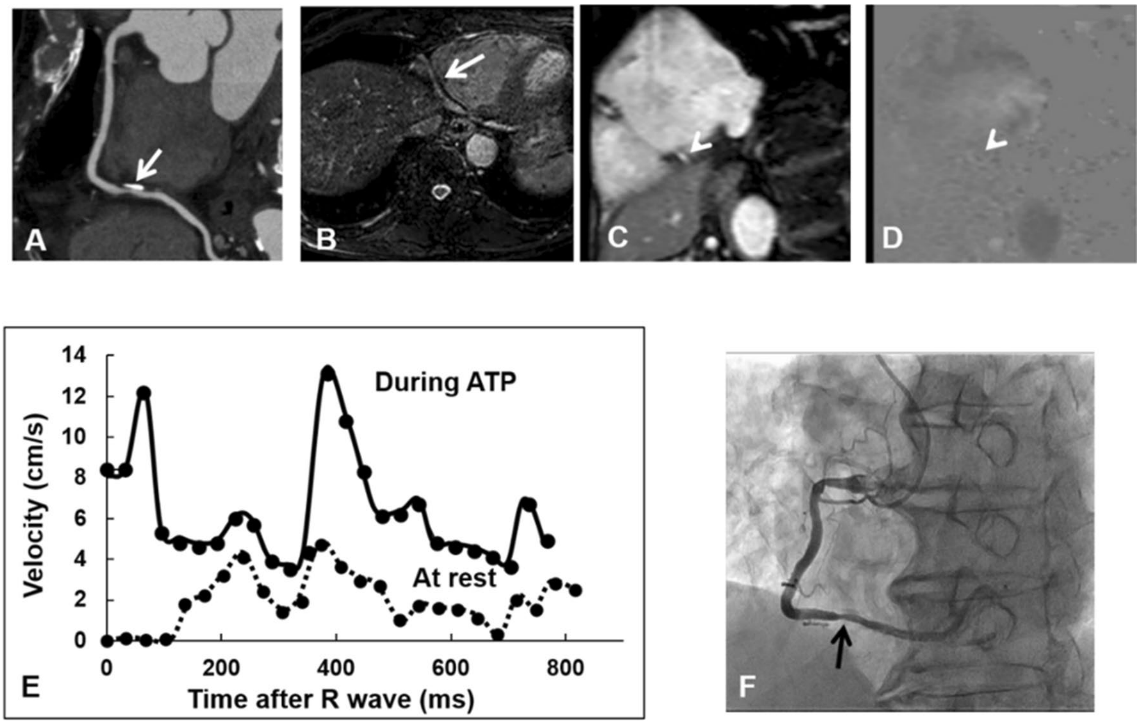

Fig. 4 (vessel case 11) In the same patient as Fig. 3, moderate stenosis was suspected in the RCA on CT angiography (**a**, arrow). **b**, MR angiography of the distal RCA is presented. Magnitude image (**c**) and phase contrast image (**d**) of the RCA distal to the suspected stenotic site. **e** Peak flow velocity was 6.5 cm/sec at rest and 15.4 during hyperemia, indicating CFVR of 2.4. On coronary angiography, mild to moderate stenosis was detected in the RCA (diameter stenosis on QCA, 48%) (**f**)

Table 3 Peak flow velocity and flow velocity reserve determined by PC-MRI in the coronary arteries

	QCA < 50%	QCA ≥ 50%	p value
Peak flow velocity (cm/s)			
At rest	9.6 ± 2.9	8.4 ± 2.4	0.36
During vasolidator stress	17.6 ± 5.0	11.0 ± 7.1	0.02
CFVR	1.9 ± 0.4	1.3 ± 0.4	0.0055

PC-MRI Phase-contrast cine magnetic resonance imaging, *CFVR* coronary flow velocity reserve, *QCA* quantitative coronary angiography

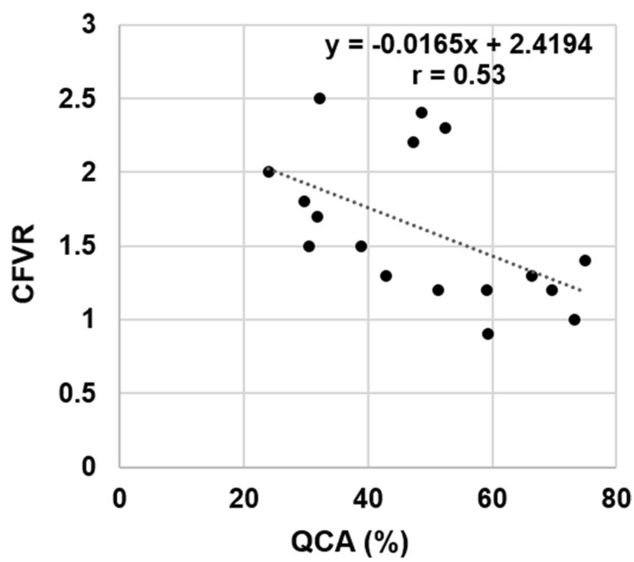

Fig. 5 The relationship between percent coronary stenosis on QCA and CFVR determined by PC-MRI. Significant moderate inverse correlation was found between percent coronary stenosis and CFVR

lead to blooming artifact, which may subsequently result in overestimation of the degree of coronary stenosis. Previous studies demonstrated that increased coronary calcifications lowered the specificity and positive predictive value of coronary CT angiography due to increased likelihood of false positive stenosis [4, 23]. On the other hand, the likelihood of coronary arterial disease increases with increasing coronary calcifications. In case of severe calcified coronary arteries, it will be crucial to decide whether to proceed to invasive X-ray angiography or choose an alternative diagnostic procedure. The current study is the first to demonstrate the value of PC-MRI to identify hemodynamically significant coronary stenosis in the cohort with heavy coronary calcification.

This study demonstrated that PC-MRI can provide incremental value for detecting significant coronary stenosis in patients with heavy coronary calcification. In this study, the positive predictive value of CT angiography for detecting ≥ 50% stenosis on QCA in patients with heavy coronary calcification was quite limited. When MRI CFVR measurements was added to CT angiography for the evaluation of coronary stenosis, false positive rates were substantially decreased (50% (8/16) vs. 13% (2/16)). In addition, high negative predictive value (89%) was observed for the evaluation of coronary stenosis by PC-MRI. These results indicate that physician may omit unnecessary coronary angiography by using PC-MRI.

The measurement of coronary blood flow with MR has been challenging because the coronary arteries are small and tortuous, and demonstrate cardiac and respiratory motion. Coronary flow velocity determined by PC-MRI can be underestimated due to the limited spatial and temporal averaging [1]. However, a previous study demonstrated that there was a good linear correlation between the coronary flow velocity measured by PC-MRI and Doppler guide wire technique [1]. Besides, our results show high agreement rates of readers for measuring CFVR (Intra-class correlation coefficient between CFVR measurements by two observers was 0.82).

High spatial resolution is necessary to accurately measure blood flow velocity in the coronary artery with PC-MRI. In the current study, the acquisition pixel size of 1.2 × 1.9 mm was employed for coronary PC-MRI. This seems to be not sufficient for accurate measurement of coronary blood flow, considering the size of coronary artery. The insufficiency in pixel size may lead to underestimate the coronary flow velocity. CFVR is determined as the ratio of rest to stress coronary flow velocity. Therefore, the influence of underestimation might be compensated to some extent.

Several limitations need to be acknowledged in this study. First, the number of subjects was limited and a larger number of subjects might be necessary to concrete our findings. However, an impaired CFVR in the stenotic coronary arteries was clearly demonstrated by the PC-MRI with sufficient inter-observer variability in the current study. Second, we did not compare the CFVR measurements by PC-MRI with other alternative functional assessment, such as CFVR determined by Doppler guide wire or fractional flow reserve. Further study is necessary to determine the diagnostic accuracy of PC-MRI for detecting hemodynamically significant coronary stenosis. Third, the test–retest reproducibility of coronary PC-MRI was not evaluated in the current study.

Conclusion

PC-MRI can provide noninvasive detection of altered CFVR caused by significant stenosis in patient with severe coronary calcification. CFVR measurement by PC-MRI is useful for diagnosing physiologically significant coronary stenosis in patients with high calcium score on CT.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

References

1. Shibata M, Sakuma H, Isaka N, Takeda K, Higgins CB, Nakano T, Assessment of coronary flow reserve with fast cine phase contrast magnetic resonance imaging: comparison with measurement by Doppler guide wire. J Magn Reson Imaging. 10(1999) 563–568. https://doi.org/10.1002/(SICI)1522-2586(199910)10:4%3C563::AID-JMRI9%3E3.0.CO;2-H
2. Hundley WG, Hills LD, Hamilton CA, Applegate RJ, Herrington DM, Clarke GD, Braden GA, Thomas MS, Lange RA, Peshock RM, Link KM. Assessment of coronary arterial restenosis with phase-contrast magnetic resonance imaging measurement of coronary flow reserve. Circulation 101(2000) 2375–2381. https://doi.org/10.1161/01.CIR.101.20.2375
3. Nagel E, Thouet T, Klein C, Schalla S, Bornstedt A, Schnackenburg B, Hug J, Wellnhofer E, Fleck E. Noninvasive determination of coronary blood flow velocity with cardiovascular magnetic resonance in patients after stent deployment. Circulation 107(2003) 1738–1743. https://doi.org/10.1161/01.CIR.0000060542.79482.81
4. Abdulla J, Pederson KS, Budoff M, Kofoed KF (2012) Influence of coronary calcification on the diagnostic accuracy of 64-slice computed tomography coronary angiography: a systemic review and meta-analysis. Int J Cardiovasc Imaging 28:943–953. https://doi.org/10.1007/s10554-011-9902-6
5. Arbab-Zeheh A, Miller JM, Rochitte CE, Dewey M, Niinuma H, Gottlieb I, Paul N, Clouse ME, Shapiro EP, Hoe J, Lardo AC, Bush DE, de Roos A, Cox C, Brinker J, Lima JA (2012) Diagnostic accuracy of computed tomography coronary angiography according to pre-test probability of coronary artery disease and severity of coronary artery calcification. The CORE-64 (Coronary Artery Tomography Angiography) international multicenter study. J Am Coll Cardiol 59:379–387. https://doi.org/10.1016/j.jacc.2011.06.079
6. Agatston AS, Janowitz WR, Hildner FJ, Zusmer NR, Viamonte M Jr, Detrano R (1990) Quantification of coronary artery calcium using ultrafast computed tomography. J Am Coll Cardiol 15:827–832. https://doi.org/10.1016/0735-1097(90)90282-T
7. Cury RC, Abbara S, Achenbach S, Agatston A, Berman DS, Budoff MJ, Dill KE, Jacobs JE, Maroules CD, Rubin GD, Rybicki FJ, Schoepf UJ, Shaw LJ, Stillman AE, White CS, Woodard PK, Leipsic JA (2016) CAD-RADS (TM) coronary artery disease – reporting and data system. An expert consensus document of the Society of Cardiovascular Computed tomography (SCCT), the American College of Radiology (ACR) and the North American Society for Cardiovascular Imaging (NASCI). Endorsed by the American College of Cardiology. J Cardiovasc Comput Tomogr 10:269–281. https://doi.org/10.1016/j.jcct.2016.04.005
8. Sakuma H, Koskenvuo JW, Niemi P, Kawada N, Toikka JO, Knuuti J, Laine H, Saraste M, Kormano M, Hartiala JJ. Assessment of coronary flow reserve using fast velocity encoded cine MR imaging: validation study using positron emission tomography.

Am J Roentgenol 175(2000) 1029–1033. https://doi.org/10.2214/ajr.175.4.1751029
9. van de Hoef TP, Nolte F, Rolandi MC, Piek JJ, van den Wijngaard JP, Spaan JA, Siebes M (2012) Coronary pressure-flow relations as basis for the understanding of coronary physiology. J Mol Cell Cardiol 52:786–793. https://doi.org/10.1016/j.yjmcc.2011.07.025
10. van de Hoef TP, van Lavieren MA, Damman P, Delewi R, Piek MA, Chamuleau SA, Voskuil M, Henrigues JP, Koch KT, de Winter RJ, Spaan JA, Siebes M, Tijssen JG, Meuwissen M, Piek JJ. Physiological basis and long-term clinical outcome of discordance between fractional flow reserve and coronary flow velocity reserve in coronary stenoses of intermediate severity. Circ Cardiovasc Interv 7(2014) 301–311. https://doi.org/10.1161/CIRCINTERVENTIONS.113.001049/-/DC1
11. Doucette JW, Corl PD, Payne HM, Flynn AE, Goto M, Nassi M, Segal J. Validation of a Doppler guide wire for intravascular measurement of coronary artery flow velocity. Circulation 85 (1992) 1899–1911. https://doi.org/10.1161/01.CIR.85.5.1899
12. Wilson RF, Laughlin DE, Ackell PH, Wilison RF, Laughlin DE, Ackell PH, Chilian WM, Holida MD, Hartley CJ, Armstrong ML, Marcus ML, White CW. Transluminal, subselective measurement of coronary artery blood flow velocity and vasodilator reserve in man. Circulation 72(1985) 82–92. https://doi.org/10.1161/01.CIR.72.1.82
13. Voudris V, Manginas A, Vassilikos V, Koutelou M, Kantzis J, Cokkinos DV (1996) Coronary flow velocity changes after intravenous dipyridamole infusion: measurements using intravascular Doppler guide wire. A documentation of flow inhomogeneity. J Am Coll Cardiol 27:1148–1155. https://doi.org/10.1016/0735-1097(95)00569-2
14. Hozumi T, Yoshida K, Akasaka T, Asami Y, Ogata Y, Takagi T, Kaji S, Kawamoto T, Ueda Y, Morioka S (1998) Noninvasive assessment of coronary flow velocity and coronary flow velocity reserve in the left anterior descending coronary artery by doppler echocardiography: comparison with invasive technique. J Am Coll Cardiol 32:1251–1259. https://doi.org/10.1016/S0735-1097(98)00389-1
15. Hozumi T, Yoshida K, Ogata Y, Akasaka T, Asami Y, Takagi T, Morioka S. Noninvasive assessment of significant left anterior descending coronary artery stenosis by coronary flow velocity reserve with transthoracic color doppler echocardiography. Circulation 97(1998) 1557–1562. https://doi.org/10.1161/01.CIR.97.16.1557
16. Szolar DH, Sakuma H, Higgins CB (1996) Cardiovascular applications of magnetic resonance flow and velocity measurements. J Magn Reson Imaging 6:78–89. https://doi.org/10.1002/jmri.1880060117
17. Lotz J, Meier C, Leppert A, Galanski M. Cardiovascular flow measurement with phase contrast MR imaging: basic facts and implementation. Radiographics 22(2002) 651–671. https://doi.org/10.1148/radiographics.22.3.g02ma11651
18. Abolmaali ND, Esmaeili A, Feist P, Ackermann H, Requardt M, Schmidt H, Vogl TJ (2004) Reference values of MRI flow measurements of the pulmonary outflow tract in healthy children. Rofo 176:837–845. https://doi.org/10.1055/s-2004-812959
19. Dandekar VK, Bauml MA, Ertel AW, Dickens C, Gonzalez RC, Farzaneh-Far A. Assessment of global myocardial perfusion reserve using cardiovascular magnetic resonance of coronary sinus flow at 3 T. J Cardiovasc Magn Reson (2014) 16:24. https://doi.org/10.1186/1532-429X-16-24
20. Ichikawa Y, Kitagawa K, Kato S, Dohi K, Hirano T, Ito M, Sakuma H (2014) Altered coronary endothelial function in young smokers detected by magnetic resonance assessment of myocardial blood flow during cold pressor test. Int J Cardiovasc Imaging 30:73–80. https://doi.org/10.1007/s10554-014-0387-y
21. Kato S, Fukui K, Kawaguchi J, Ishii N, Koga M, Kusakawa Y, Kusama I, Nakachi T, Nakagawa T, Terauchi Y, Uchino K, Kimura K, Umemura S (2013) Relationship between coronary flow reserve evaluated by phase-contrast cine cardiovascular magnetic resonance and serum eicosapentaenoic acid. J Cardiovasc Magn Reson 15:106. https://doi.org/10.1186/1532-429X-15-106
22. Kreitner KF, Ehrhard K, Kunz RP, Abegunewardene N, Oberholzer K, Horstick G, Hake U, Mildenberger P, Thelen M (2004) Non-invasive assessment of coronary artery bypass grafts an update. Rofo 176:1079–1088. https://doi.org/10.1055/s-2004-813278
23. Kuettner A, Kopp AF, Schroeder S, Rieger T, Brunn J, Meisner C, Heuschmid M, Trabold T, Burgstahler C, Martensen J, Schoebel W, Selbmann HK, Claussen CD (2004) Diagnostic accuracy of multidetector computed tomography coronary angiography in patients with angiographically proven coronary artery disease. J Am Coll Cardiol 43:831–839. https://doi.org/10.1016/j.jacc.2003.05.015