Three-Dimensional Black-Blood Cardiac Magnetic Resonance Coronary Vessel Wall Imaging Detects Positive Arterial Remodeling in Patients With Nonsignificant Coronary Artery Disease

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Background—Direct noninvasive visualization of the coronary vessel wall may enhance risk stratification by quantifying subclinical coronary atherosclerotic plaque burden. We sought to evaluate high-resolution black-blood 3D cardiovascular magnetic resonance (CMR) imaging for in vivo visualization of the proximal coronary artery vessel wall.

Methods and Results—Twelve adult subjects, including 6 clinically healthy subjects and 6 patients with nonsignificant coronary artery disease (10% to 50% x-ray angiographic diameter reduction) were studied with the use of a commercial 1.5 Tesla CMR scanner. Free-breathing 3D coronary vessel wall imaging was performed along the major axis of the right coronary artery with isotropic spatial resolution (1.0 × 1.0 × 1.0 mm³) with the use of a black-blood spiral image acquisition. The proximal vessel wall thickness and luminal diameter were objectively determined with an automated edge detection tool. The 3D CMR vessel wall scans allowed for visualization of the contiguous proximal right coronary artery in all subjects. Both mean vessel wall thickness (1.7 ± 0.3 versus 1.0 ± 0.2 mm) and wall area (25.4 ± 6.9 versus 11.5 ± 5.2 mm²) were significantly increased in the patients compared with the healthy subjects (both \( P < 0.01 \)). The lumen diameter (3.6 ± 0.7 versus 3.4 ± 0.5 mm, \( P = 0.47 \)) and lumen area (8.9 ± 3.4 versus 7.9 ± 3.5 mm², \( P = 0.47 \)) were similar in both groups.

Conclusions—Free-breathing 3D black-blood coronary CMR with isotropic resolution identified an increased coronary vessel wall thickness with preservation of lumen size in patients with nonsignificant coronary artery disease, consistent with a “Glagov-type” outward arterial remodeling. This novel approach has the potential to quantify subclinical disease.

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Key Words: atherosclerosis • plaque • vessels • magnetic resonance imaging

Coronary magnetic resonance angiography (MRA) allows for the noninvasive assessment of significant coronary artery luminal stenosis. However, assessment of coronary lumen integrity is of limited value for the detection of subclinical coronary artery disease (CAD) because at the early stages of atherosclerosis, the coronary artery lumen is usually preserved by outward (positive) arterial remodeling, known as the Glagov effect. It is of clinical importance to recognize subclinical CAD because acute coronary syndromes frequently result from rupture of an atherosclerotic plaque in an area of only mild-to-moderate luminal narrowing.

We have recently implemented a black-blood three-dimensional (3D) cardiovascular magnetic resonance (CMR) sequence with isotropic image resolution to enable vessel wall imaging along the major axis of the proximal coronary arteries. In the present study, we sought to determine whether this novel approach can detect outward arterial remodeling (by means of an increased coronary wall thickness) in patients with subclinical CAD.

Methods

Subjects

The study population included 6 clinically healthy adult subjects without known cardiac disease (2 males and 4 females; aged 33 ± 12 years, range 25 to 57 years) and 6 patients (4 males and 2 females; aged 67 ± 10 years, range 54 to 79 years) with nonsignificant stenoses (10% to 50% diameter reduction) by x-ray coronary angiography.

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Movies I and II are available in an online-only Data Supplement at http://www.circulationaha.org.

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angiography. One patient had been referred for x-ray angiography before heart valve replacement, whereas the others were referred for evaluation of suspected CAD. Coronary MRA and CMR vessel wall imaging of the right coronary artery (RCA) were performed in all subjects. All subjects were in sinus rhythm, without contraindications to CMR exams, and provided written informed consent.

CMR Imaging Procedure
The CMR examination was performed on a commercial 1.5 Tesla system (Gyroscan ACS-NT 15, Philips Medical Systems) equipped with PowerTrak 6000 gradients (23 mT/m, 219 μs rise time). All subjects were examined in the supine position with the use of a commercial 5-element cardiac synergy receiver coil. All coronary scans were performed with cardiac synchronization during free breathing with the use of a navigator technique.8

Localization of the Coronary Arteries
A plane through the major axis of the proximal RCA was identified with the use of a 3-point planscan tool to define the course of the proximal coronary arteries as depicted from a transverse 3D scan positioned about the base of the heart.7

Three-Dimensional Coronary MRA
Double oblique 3D bright-blood coronary MRA of the RCA was performed along the formerly identified long axis of the proximal coronary artery by use of an ECG-gated TFE/EPI sequence (repetition time [TR]=16 ms, echo time [TE]=5.1 ms, 3 excitations per shot, flip angle=40°, EPI factor=7, acquisition window 33 ms, field of view [FOV]=340 mm, scan matrix=256×177, in-plane resolution=1.3×1.9 mm², reconstructed slice thickness 1.5 mm, 21 slices).8 The total acquisition time for this scan was ~3 minutes.

Three-Dimensional CMR Vessel Wall Imaging
The black-blood 3D CMR wall scan was performed in the same imaging plane as the 3D bright-blood coronary MRA. The black-blood properties were obtained with a modified local dual-inversion prepulse to null signal from blood and surrounding tissue.5 To suppress the signal from epicardial fat, a frequency-selective fat suppression prepulse was applied. A 3D spiral imaging sequence5 was used for the vessel wall imaging (TR=30 ms, TE=2 ms, acquisition window 60 ms, 26 slices with a thickness of 1 to 2 mm, FOV 400 to 512 mm, acquisition matrix 512×512, in-plane resolution 0.78 to 1.0×0.78 to 1.0 mm). The imaging time for this scan was ~15 minutes.

Coronary Vessel Wall and Lumen Evaluation
For evaluation of the coronary vessel wall and lumen size, the 3D CMR vessel wall and coronary MRA datasets were reformatted along the major axis of the RCA on a commercial workstation (EasyVision 4.0, Philips Medical Systems). To minimize digitization errors and facilitate data analysis, the images were zoomed by a factor of 4 with the use of a fast Fourier transform algorithm.9 The errors and facilitate data analysis, the images were zoomed by a factor of 4 with the use of a fast Fourier transform algorithm.9 The average proximal vessel wall thickness and average luminal diameter along the entire visualized course of the RCA (inner and outer curvature) (Figures 1 and 2) were objectively determined with an automated edge-detection tool.10

To visualize the whole circumference of the vessel wall, an animated sequence of cross-sectional views was generated (Movies I and II) from the 3D dataset perpendicular to the major axis of the vessel. On cross-sectional images of the RCA, the inner lumen and outer vessel borders were then manually segmented to determine coronary lumen and wall area.11 The average area values were calculated from 4 equidistant cross-sectional images measured at 10-mm intervals.

Statistics
Continuous variables in patients and healthy subjects were compared with the use of a Wilcoxon rank-sum test, with significance at $P<0.05$. The wall thickness was correlated by a linear regression analysis to the lumen diameter.

Results
All subjects completed CMR examination without complications. The 3D CMR vessel wall scans allowed for visualization of the contiguous proximal RCA in all patients and healthy subjects ($52±13$ versus $57±10$ mm, $P=0.47$). The coronary vessel wall appeared distinct from the surrounding epicardial fat and coronary blood (black lumen), and the 2D local dual-inversion pulse effectively suppressed unwanted signals outside the region of interest (Figures 1 and 2). Average signal-to-noise ratio of the RCA wall was similar for patients ($35±11$) and healthy subjects ($36±18$, $P=0.58$). The contrast-to-noise ratio between RCA wall/epicardial fat was $21.7$ in the patients and $17±11$ in the healthy subjects ($P=0.23$). The contrast-to-noise ratio between RCA wall/cor-

Figure 1. Reformatted 3D coronary MRA (A) and local dual-inversion black-blood (B) vessel wall scans of the RCA in a healthy subject. Cross-sectional views at 3 levels are also shown (I, II, III).

Figure 2. X-ray angiography in 2 patients with (A) a focal 40% stenosis (white arrow) and (C) minor (~10% stenoses) luminal irregularities (white arrows) of the proximal RCA. The corresponding black-blood 3D CMR vessel wall scans (B, D) demonstrate an irregularly thickened RCA wall (>2 mm) indicative of an increased atherosclerotic plaque burden. The inner and outer RCA walls are indicated by the white dotted arrows. The catheter size for the x-ray was 6F.
Coronary blood was also similar for patients (23±10) and healthy subjects (24±8, P=0.81).

In the healthy subjects, the coronary wall appeared uniformly thin with homogenous signal intensity (Figure 1, Movie I). In the patients, focal thickening of the wall was noted especially at sites corresponding to luminal narrowing on the x-ray angiogram (Figure 2, Movie II).

Both mean vessel wall thickness (Figure 3) (1.7±0.3 versus 1.0±0.2 mm) and wall area (25.4±6.9 versus 11.5±5.2 mm²) were significantly increased in the patients with nonsignificant CAD compared with the healthy subjects (both P<0.01). The lumen diameter (Figure 4) (3.6±0.7 versus 3.4±0.5 mm, P=0.47) and lumen area (8.9±3.4 versus 7.9±3.5 mm², P=0.47) were similar in patients and healthy subjects. Thus, the ratio of coronary lumen/wall dimension was significantly reduced in the patients compared with healthy subjects (2.1±0.3 versus 3.7±0.9, P<0.01). There was no significant correlation (P=0.14) between vessel wall thickness and coronary MRA lumen diameter for the pooled data.

**Discussion**

Our results demonstrate that the CMR approach identified an increased coronary vessel wall thickness with preservation of lumen size in patients with nonsignificant CAD, consistent with a Glagov-type outward arterial remodeling process. Outward or positive remodeling denotes an increase in total vessel size, whereas inward remodeling denotes a decrease in vessel size. The concept of arterial remodeling as a compensatory response to atherosclerotic plaque growth has previously been observed exclusively from postmortem or intravascular ultrasound studies. The critical importance of arterial remodeling and not plaque size as the primary determinant of lumen size in the presence of stable atherosclerotic lesions has only recently been recognized. Furthermore, evidence that outward (rather than inward) arterial remodeling is more often associated with morphological predictors of plaque instability, and plaque rupture with subsequent acute coronary syndrome has stimulated clinical interest in developing CMR as a noninvasive method to allow for serial studies of arterial remodeling in humans.

Other investigators who used 2D high-resolution transthoracic echocardiography found a significant increase in the left anterior descending (LAD) vessel wall thickness in patients with CAD compared with healthy subjects. Previous studies that used 2D black-blood CMR vessel wall imaging showed the potential of CMR to detect an increased wall thickness and wall area in patients with angiographically significant CAD. In the present study, we focused on visualization of the RCA, though we have previously demonstrated the feasibility of this CMR approach for the LAD. The impact of spatial resolution on CMR evaluation of coronary atherosclerotic plaque burden was investigated showing that the current spatial resolution of 0.8 to 1×0.8 to 1×1 to 2 mm³ is associated with a relative overestimation of the wall area of ~30% to 40% in patients versus 50% to 60% in healthy subjects. The proximal RCA wall thickness was measured by objective analysis along the entire visualized course and averaged to distinguish sub-pixel changes. The reported values of wall thickness therefore reflect the wall thickness throughout the vessel. The very irregular nature of wall thickening and the presence of minor x-ray angiographic luminal stenosis in all patients suggest that the increased wall thickness represents atherosclerosis. With the use of 2D echocardiography, other investigators have not found any systematic effect of age on wall thickness and external vessel diameter in healthy subjects or patients with CAD.

Though unproven by the present study, CMR assessment of coronary wall thickness may prove useful for improved risk stratification in individual patients, thereby guiding early treatment and ultimately preventing acute coronary events. In addition, the natural history of coronary atherosclerosis could be studied noninvasively to further our understanding of the complex relationship between arterial remodeling, vessel inflammation, and plaque rupture.

**References**

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