Objectives
We examined whether delayed-enhancement cardiovascular magnetic resonance (DE-CMR) coronary artery wall imaging correlated with atherosclerosis detected by using multislice computed tomography (MSCT) and quantitative coronary angiography (QCA).

Background
The use of DE-CMR coronary vessel wall imaging may provide a noninvasive method to assess diseased coronary vessel walls.

Methods
We performed DE-CMR coronary artery wall imaging in 14 patients with cardiovascular risk factors and 6 healthy subjects without risk factors.

Results
A greater prevalence of strong DE was noted with greater MSCT evidence of disease, with DE in 2 (7%) of 30 coronary segments with no plaque by MSCT, in 1 (10%) of 10 segments with noncalcified plaque on MSCT, and in 16 (36%) of 44 segments with calcifications by MSCT (p = 0.009, adjusted p = 0.035). Delayed enhancement was observed in 8 (53%) of 15 segments with >20% coronary artery stenosis by QCA but also in 12 (15%) of 80 segments without angiographically apparent coronary disease (p = 0.004, adjusted p = 0.01).

Conclusions
The use of DE-CMR allowed us to identify areas of DE that correlate with severity of atherosclerosis by MSCT and QCA. This novel approach may be useful for the assessment of coronary vessel wall in patients with suspected coronary artery disease. (J Am Coll Cardiol 2007;50:441–7) © 2007 by the American College of Cardiology Foundation

Multislice computed tomography (MSCT) (1–4) and cardiovascular magnetic resonance (CMR) imaging (5–7) have emerged as promising noninvasive imaging techniques for coronary plaque visualization. Noncontrast CMR coronary vessel wall imaging enables the identification of thickened coronary wall (5–7) but requires high spatial resolution and accurate motion correction. Contrast-enhanced CMR may provide an alternative because it is useful for evaluating carotid (8–11) and aortic (9,12) plaque. Delayed-enhancement (DE) CMR (13) simplifies the imaging task to detection of contrast uptake, thereby slightly reducing spatial resolution requirements. An earlier preliminary study suggested that DE-CMR may be useful for coronary plaque imaging, although significance of findings in relation to other plaque assessment was not evaluated (14). In the current study, we sought to determine whether DE-CMR coronary vessel wall imaging findings correlate with atherosclerosis detected by MSCT and quantitative coronary angiography (QCA). In addition, DE-CMR results for healthy control subjects were assessed.

Methods
Patients. Fourteen subjects (age 63 ± 9 years, range 46 to 76 years; 10 men) with one or more coronary risk factors...
(diabetes mellitus, hypertension, hyperlipidemia, family history of premature coronary artery disease, cigarette smoking) who had undergone X-ray coronary angiography (CATH) and MSCT were enrolled. In addition, 6 healthy control subjects (age 25 ± 7 years, range 19 to 33 years; 2 men) with no risk factors (and no CATH or MSCT) were enrolled. The study protocol was approved by the institutional board on clinical investigations at Beth Israel Deaconess Medical Center. Written informed consent was obtained from all subjects.

CMR imaging. Subjects were scanned in the supine position on a 1.5-T CMR scanner (Gyroscan ACS-NT, Philips Medical Systems, Best, the Netherlands) with 5-element cardiac synergy coil and advanced cardiovascular software package (R9.1).

Coronary CMR imaging. Coronary MR angiography of the right and left coronary artery systems were imaged using a previously described free-breathing electrocardiogram-triggered 3-dimensional balanced steady-state free precession coronary magnetic resonance imaging sequence (15). Imaging parameters included field of view = 320 mm, matrix = 256 × 256, in-plane resolution = 1.25 × 1.25 mm, slice thickness = 3 mm, acquisition window = 80 to 100 ms, TR/TE = 5.4 ms/2.7 ms, flip angle = 110°, start up cycles = 5, and number of slices = 12 to 15.

Coronary artery wall imaging with DE-CMR. Approximately 60 min before vessel wall imaging, 0.2 mmol/kg of gadolinium-DTPA (Magnevist, Berlex Laboratories, Montville, New Jersey) was administered intravenously. We performed DE-CMR coronary artery wall imaging using a T1-weighted 3-dimensional gradient echo inversion recovery sequence (3D IR TFE) (16,17). Imaging parameters, including imaging plane and voxel size, were identical to the coronary MRI sequence, except for TR/TE = 6.1/1.9 ms, flip angle = 30°, and an inversion RF pulse instead of T2prep for magnetization preparation (inversion time adjusted to null blood, typically ~280 ms). Subjects with visually evident coronary artery wall DE were asked to return for a second imaging session (>60 h after the first scan) for noncontrast (“native”) CMR vessel wall imaging using the same imaging parameters. Inversion time was again adjusted to null blood (typically inversion time ~400 ms).

Modeling of pharmacokinetics. To estimate T1 values over time, simulations were made based on earlier published values of plasma concentration of Gd-DTPA at various time points following intravenous injection in humans (18). Contrast agent clearance from vessel wall was assumed to be 3- to 5-fold slower than for blood, and plaque was modeled to contain a blood fraction of 80%. The optimal inversion time for minimizing blood signal was estimated as a function of heart rate, contrast agent dose, and time after injection using the T1 values derived from the simulation.

In 5 subjects, the results of the simulation were confirmed by comparison with data obtained with a Look-Locker sequence (19). Similarly, the optimal imaging time point after contrast administration was derived by evaluating the temporal behavior of blood to vessel wall contrast for different contrast doses.

MSCT coronary angiography. Multislice computed tomography (for 11 subjects: 16-row, Aquilion 16, Toshiba America Medical Systems, Tustin, California; for 3 subjects: 64-row, Aquilon 64) was performed after administration of 90 ml of nonionic contrast agent (ioversol, Optiray 350, Tyco Healthcare, Mansfield, Massachusetts). Subjects with heart rates >70 beats/min received intravenous meto-
prolol. Scan parameters for 16-row imaging included slice thickness = 0.5 mm, field of view = 320 mm, image matrix 512 × 512, pixel size 0.39 mm², gantry rotation time 0.4 s, 135 kVp, 350 mA, and total scan time 16 to 24 s (3). Radiation dose was 11.4 mSv as calculated using IMPACT software (IMPACT Scan, London, United Kingdom). Scan parameters for 64-row imaging included slice thickness 0.5 mm, field of view = 320 mm, image matrix 512 × 512, pixel size 0.39 mm², gantry rotation time = 0.4 s, 135 kVp, 350 mA with a total scan time of 8 to 9 s (3). Radiation dose was 17.8 mSv as calculated using IMPACT software.

**CATH.** The subjects who had been referred for CATH by their treating physicians underwent conventional CATH (after MSCT and before DE-CMR) using standard techniques with multiple projections (20).

**Image analysis.** Image analyses were performed for each of 7 coronary segments, including the left main, and the proximal and mid left anterior descending, left circumflex, and right coronary arteries. For uniform segment identification, segments were predefined according to distance from coronary artery origin rather than by branch vessel location.

**DE-CMR image analysis.** The DE-CMR image analyses were performed by an investigator who was blinded to other data on multiplanar reformatted images using a previously described analysis package (21). Contrast-to-noise (CNR) between coronary vessel wall and aortic blood (at the origin of left main and right coronary artery) was determined. Segments were categorized quantitatively on a 3-point scale with 0 = no (CNR ≤ 2), 1 = moderate (2 < CNR < 7), and 2 = strong enhancement (CNR ≥ 7).

**MSCT image analysis.** The MSCT images were analyzed on a dedicated 3D workstation (Vitrea 2, Version 3.5 Vital Images Inc, Plymouth, Minnesota). Images were recon-
structured with slice thickness of 0.4 mm using a medium sharp convolution kernel at 10% intervals. Images were reviewed by an observer who was blinded to other data (3,22). Automatic vessel detection with manual correction was used to display multiplanar reformations and orthogonal cross-sectional coronary views (23). The presence and location of noncalcified (<130 HU), mildly to moderately calcified (130 to 400 HU), and (>400 HU) severely calcified plaque was assessed (2,24).

**QCA analysis.** QCA analysis was performed by an independent observer who was blinded to other data. These analyses were performed according to standard algorithms to measure lesion stenosis with respect to mean reference diameter (25).

**Statistical analysis.** The DE-CMR data were compared with the reference standards of presence of coronary plaque detected by MSCT and >20% luminal narrowing by QCA. The relationship between strong DE and the results of QCA and MSCT were evaluated using the Fisher exact test, assuming independence of each vessel segment. Generalized estimating equations were used to adjust these results to account for correlation between repeated measurements in the same individual. Continuous data are expressed as mean ± 1 SD. Categorical data are expressed as counts and percentages. Continuous variables were compared using a 2-tailed, paired, Student t test. A p value of 0.05 was used to determine statistical significance.

**Results**

Patient characteristics are summarized in Table 1. No subject had an acute coronary syndrome. All patients completed DE-CMR, allowing for CMR assessment of 91 (93%) of 98 coronary segments in 14 subjects (3 segments not evaluated because of the presence of stents, 4 segments not evaluated because of suboptimal image quality). A total of 81 of these segments were able to be evaluated with MSCT. Suppression of blood signal (mean SNR = 3.4 ± 1.2; range 1.6 to 6.9) was good in most subjects (Figs. 1 to 3), allowing good delineation of the vessel wall in patients with coronary artery disease (Figs. 2 and 3). No DE was observed in the coronary wall or thoracic aortic wall in any of the healthy control subjects (Fig. 1).

Figures 2 and 3 show representative images comparing CMR, MSCT, and CATH and demonstrate the correspondence of findings. In 2 (25%) of 8 patients with CMR...
contrast enhancement and coronary artery disease risk factors returning for native CMR vessel wall imaging, 3 (5%) focal hyperintense areas were found on noncontrast images of 64 segments. On MSCT, 2 mildly to moderately and 1 severely calcified plaque was found at the corresponding location. All locations of native hyperintensity correlated with ≥50% stenoses on QCA. Among the 11 of 14 patients having coronary artery wall DE, on average, 4.6 (66%) of 7 evaluable coronary segments showed DE. There was progressive increase in the prevalence of strong DE-CMR with increasing MSCT atherosclerotic burden (Fig. 4). Strong CMR DE was noted in 2 (7%) of 30 coronary segments with no plaque by MSCT, in 1 (10%) of 10 segments with noncalcified plaque, and in 16 (36%) of 44 segments with calcified plaque (p = 0.009, adjusted p = 0.035).

Strong CMR DE was observed in 8 (53%) of 15 segments with >20% coronary artery stenosis by QCA but also in 12 (15%) of 80 segments without angiographically apparent coronary disease (p = 0.004, adjusted p = 0.01) (Fig. 5). Of 14 QCA stenotic segments evaluated by MSCT, 1 (7%) contained no detected plaque, 2 (14%) contained noncalcified plaque, 1 (7%) mildly to moderately calcified plaque, and 9 (64%) severely calcified plaque.

Discussion. In this study, we compared DE-CMR results to coronary plaque detection by MSCT and >20% luminal narrowing by QCA. In subjects with coronary atherosclerosis (>20% lumen stenosis), DE-CMR coronary plaque
imaging enabled selective plaque visualization (8 of 15 segments; 53%) distinct from vessel wall depiction observed with native black blood coronary vessel wall imaging. Contrast uptake was more often observed in calcified (36%) than in noncalcified plaques (10%) or segments without plaque (7%). No DE-CMR vessel wall enhancement was observed in any healthy control subject. DE-CMR contrast uptake may be associated with an increased distribution volume (as with fibrosis and neovascularization) in the altered vessel wall or with increased vascular permeability (as may occur with inflammation).

**Distribution of coronary vessel wall DE-CMR.** When coronary segments were classified according to MSCT-defined plaque type, there was a greater prevalence of strong enhancement among segments with noncalcified plaques than among segments without plaque and an even higher prevalence among calcified plaques. Segments with calcified plaques by MSCT were likely to display strong enhancement (36%), but there were also a sizable minority of MSCT calcified segments that demonstrated no or only moderate enhancement (36% and 27% respectively). Thus, the sensitivity of DE-CMR to detected calcified plaque was limited. Calcific elements may be superimposed upon fibrous plaque components developing with chronic vascular inflammation. Such fibrous elements may be detected by contrast enhancement as has been demonstrated in carotid disease (8,11).

Native hyperintensity was observed in 3 calcified plaques by MSCT, which were all found to be stenotic (≥50%) on QCA. One explanation for this observation may be the presence of mural or intraplaque thrombus containing methemoglobin, which is known to have a short T1 relaxation time (26). Of note, “native” imaging was performed >60 h after contrast injection. According to the pharmacokinetics of Gd-DTPA, a complete blood clearance is expected after 400 min (18). Assuming a 5-fold slower washout in coronary plaque, a complete clearance is expected after 34 h. However, the possibility that enhancement could persist at >60 h after Gd-DTPA injection cannot be excluded.

**Diffuse versus focal enhancement.** In an autopsy study (27) of patients dying of acute myocardial infarction, diffuse and active coronary inflammation was found together with focal manifestations of atherothrombosis. In our study, ~53% of coronary artery segments displayed at least moderate DE, which is consistent with studies indicating the diffuse nature of coronary artery disease (27,28). The DE-CMR technique may help assess coronary vessel wall changes which may be more widespread than luminal lesions.

**Control group.** DE-CMR was not observed in any of our healthy control subjects. This negative finding is in agreement with the likely absence of coronary atherosclerosis in young subjects without cardiovascular risk factors.

**Study limitations.** The number of subjects in this study is small. We did not compare DE-CMR with intravascular ultrasound, which is the current in vivo gold standard for coronary plaque assessment. However, intravascular ultrasound is an invasive technique with associated non-negligible risks. Furthermore, no comparison with histopathologic data was performed. Another limitation of this study is that some segments were not evaluable by CMR (7 of 98 segments [7%] and 10 of the remaining 91 segments [11%] were not evaluable by MSCT). The 10 segments that were unevaluable by MSCT were in 4 subjects studied by 16-row scans.

**Conclusions**

We demonstrated successful application of DE-CMR for plaque visualization in the major epicardial coronary arteries and demonstrate increasing prevalence of DE-CMR coronary artery wall contrast enhancement with increasing severity of plaque calcification by MSCT and correlation with lumen stenosis by CATH. This approach may prove useful for the assessment of coronary disease in patients with subclinical and advanced atherosclerosis. Future work will be directed toward further defining vessel wall characteristics in selected patient groups and identifying clinical factors associated with coronary wall contrast enhancement.

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**REFERENCES**


