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LETTER TO THE EDITOR

Contrast Enhancement Imaging in Coronary Arteries in SLE

The basis of gadolinium enhancement imaging by cardiovascular magnetic resonance (CMR) is the gadolinium accumulation within the extracellular space (1). Increased extracellular space in the coronary vessel wall can be visualized by contrast-enhanced inversion-recovery (CE-IR) prepared coronary imaging as an increased contrast uptake (2). In patients with stable angina, there is increased enhancement within complex atherosclerotic plaques. In patients with acute coronary syndrome, increased coronary enhancement was found 3 to 7 days post-event but ameliorated after 3 months (2,3). Demonstration of subclinical coronary involvement can be potentially useful in patients where an excess of systemic inflammation promotes accelerated atherosclerotic remodeling. Patients with systemic lupus erythematosus (SLE) suffer from an increased rate of coronary events, which are frequently clinically silent (4). Despite abundant evidence for increased systemic atherosclerotic burden in these patients, there is no direct evidence of subclinical involvement of coronary vessels. We hypothesized that CE-IR CMR can be used to visualize coronary wall changes in patients with systemic inflammation.

Nineteen subjects (men = 4) with known diagnosis of SLE were recruited from a dedicated rheumatology service. All patients were in clinical remission with stable blood results and no change in medication within the previous 8 weeks. Age/sex-matched, apparently healthy subjects (n = 9, men = 3) without angiographically detectable coronary artery disease (CAD) within the previous 3 months served as control subjects. Criteria of exclusion were history of cardiac events, known CAD, or contraindication to CMR. The study proto-

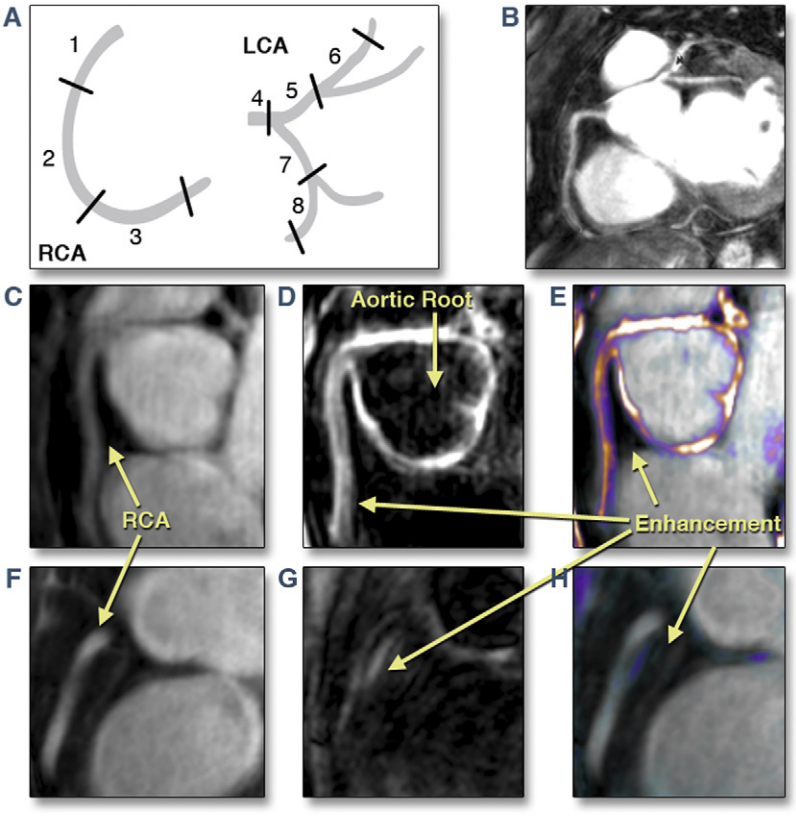

Figure 1. Anatomical and Morphological Relationships in Epicardial Coronary Tree

Segmental model of epicardial coronary artery tree **(A)** and a scout 3-dimensional coronary angiography **(B)**. **(C to E)** Representative images of right coronary artery (RCA) from a 38-year-old female patient with systemic lupus erythematosus and **(F to H)** from age/sex-matched healthy subject. **(C and F)** Cardiac magnetic resonance coronary angiography with luminogram, used to measure vessel length and lumen diameter. **(D and G)** Contrast-enhanced inversion-recovery images with black-blood pre-pulse to null the blood signal and reveal enhancement within aortic and coronary vessel wall. **(E and H)** Fused images of both previous ones to depict enhancement **(orange)** in relation to vessel lumen **(bright signal)**. LCA = left coronary artery.

Table 1. Subject Characteristics and Medication

	Control Subjects (n = 9)	SLE (n = 19)
Age, yrs	40 (26–51)	41 (24–54)
Hypertension	6 (67)	13 (68)
Males	2 (22)	4 (21)
Positive family history of cardiovascular disease	2 (22)	5 (26)
Smoking	3 (33)	6 (32)
Total cholesterol (mmol/l)	4.7 ± 1.8	4.8 ± 1.1
HDL cholesterol (mmol/l)	1.4 ± 0.6	1.0 ± 0.3*
Glucose (mg/dl)	5.7 ± 2.1	6.0 ± 1.9
Albumin (mg/dl)	42.0 ± 2.8	42.2 ± 3.6
eGFR (ml/min)	102.0 ± 7.0	86.1 ± 21.0*
Leukocytes (n × 103/μl)	8.3 ± 2.1	6.1 ± 2.5
C-reactive protein (mg/l)	2.4 ± 1.2	5.2 ± 3.8*
Erythrocytes sedimentation rate (mm/h)	<7	32.0 ± 37.4†
Medication		
Prednisolone—current use	—	17 (89)
Dose (mg/day, range)	—	7.9 (2.5–20)
Mycophenolate mofetil	—	11 (58)
Hydroxychloroquine	—	11 (58)
Methotrexate	—	4 (21)

Values are n (range), n (%), or mean ± SD. Student *t* test; *p < 0.05; †p < 0.01.
HDL = high-density lipoprotein; eGFR = estimated glomerular filtration rate (mean ± SD; SLE = systemic lupus erythematosus.

col was approved by the Institutional Review Board, and written informed consent was obtained from all participants.

Standard CMR imaging for cardiac volumes/mass and myocardial scar was performed in all subjects (3T Achieva, Philips Healthcare, Best, the Netherlands). To allow sufficient washout of the gadolinium from the blood pool, coronary studies were performed 40 min after intravenous injection of 0.2 mmol/kg gadobutrol (Gadovist, Bayer Healthcare, Germany). Coronary imaging and analysis was previously described in detail (2,3). In brief, the coronary arteries were localized with a 3-dimensional T2-prepared fast-gradient-echo scan. Double-oblique targeted volume coronary CMR angiography was performed parallel to the left and right coronary artery system (1). For CE-IR coronary artery wall imaging, a T1-weighted 3-dimensional gradient echo inversion recovery sequence with a patient-specific inversion time to null the blood signal was used. Quantitative analysis of the coronary images was by vessel tracing and edge detection on gray-scale images (coronary artery length and diameter). Coronary wall enhancement was determined as the contrast/noise ratio of signal intensities (SI) of blood pool and vessel wall corrected for the noise level (CNR = [SIwall − SIblood]/SD noise) (Fig. 1). Blood SI was determined from a region of interest in the ascending aorta at the level of the left main stem. Coronary wall SI was assessed within proximal coronary segments by multiple sampling in the long-axis coronary views. Noise was determined in a region of interest placed ventrally to the chest wall of the patient. Mean differences between the groups were identified by Student *t* tests; all tests were 2-sided.

Patient characteristics are presented in Table 1. Median duration of condition was 7 years, and the typical age at the diagnosis was 26 years. The average vessel length to determine coronary CNR was 4.2 cm (95% confidence interval [CI]: 1.7 to 8.6); left coronary artery (LCA): 4.1 cm (95% CI: 0.65 to 6.9, n = 11); right coronary artery (RCA): 4.3 cm (95% CI: 0.45 to 9.6, n = 16). Mean coronary diameter was reduced in SLE patients (control subjects vs. SLE [mm]: 2.5 ± 0.8 vs. 1.9 ± 0.6, p < 0.01 for RCA; and 2.9 ± 0.9 vs. 2.3 ± 0.5, p = 0.03 for LCA). The ratios between minimum/mean diameters were similar in both groups (healthy subjects vs. SLE: RCA: 84% vs. 76% p = 0.42; LCA: 78% vs. 75%, p = 0.91). Coronary CNR was significantly increased in SLE subjects compared with control subjects (3.9 ± 0.9 vs. 7.7 ± 2; p < 0.001). Receiver-operating characteristics analysis revealed an absolute CNR cutoff of 5.2 to discriminate healthy control subjects from the patients, resulting in 100% sensitivity and specificity. Using the value of 2 SD above the mean of the control group resulted in a cutoff value of 6.6 with 52% sensitivity and 100% specificity.

Our study reveals a subclinical involvement of the coronary vessel wall in SLE patients. We demonstrate, by visualization of the gadolinium uptake in the vessel wall, an increased extracellular space in coronary vessel walls in subjects with SLE and a history of systemic inflammation.

A CE-IR CMR was successfully applied previously for plaque characterization in arteries of various calibers, including complex plaque and neovascularization in patients with advanced carotid disease and CAD. Contrast uptake has also been shown in inflammatory involvement in giant cell arteritis and Takayasu aortitis (5). Previous studies of coronary enhancement focused on patients with CAD, comparing diseased vessels with non-diseased vessels within the same patient. Our study relates patient findings to matched control subjects and, despite a small sample, provides a first estimation of normal values. Further studies are needed to establish sex and age reference ranges of coronary enhancement. Our study is also the first to provide evidence of coronary vessel wall involvement in patients with SLE and longstanding systemic inflammation. Contribution, if any, of concomitant long-term steroid and disease modifying therapy to these observations remains unknown. The patterns of distribution of coronary enhancement seem to be condition related; segmental pattern in giant-cell arteritis by inflammation and patchy distribution in CAD both contrast the widespread coronary enhancement in SLE (2–4). Because SLE patients were asymptomatic from a cardiac viewpoint and showed no myocardial scarring, evidence of coronary enhancement might hold a potential for a surrogate of subclinical disease, especially when cardiovascular (CV) risk assessment is challenging and not resolved by classical risk stratification scores. Further studies are needed to validate and translate coronary wall enhancement as an independent marker or surrogate parameter of poor CV prognosis.

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