Journal of the American College of Cardiology
© 2014 by the American College of Cardiology Foundation
Published by Elsevier Inc.

Vol. 63, No. 10, 2014
ISSN 0735-1097/$36.00
http://dx.doi.org/10.1016/j.jacc.2013.11.034

Cardiac Imaging

High-Intensity Signals in Coronary Plaques on Noncontrast T1-Weighted Magnetic Resonance Imaging as a Novel Determinant of Coronary Events

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Objectives The aim of this study was to determine whether coronary high-intensity plaques (HIPs) visualized by noncontrast T1-weighted imaging can predict future coronary events.

Background Coronary HIPs are associated with characteristics of vulnerable plaques, including positive remodeling, lower Hounsfield units, and ultrasound attenuation. However, it remains unclear whether the presence of HIPs is associated with increased risk for coronary events.

Methods The signal intensity of coronary plaques was prospectively examined in 568 patients with suspected or known coronary artery disease (CAD) who underwent noncontrast T1-weighted imaging to determine the plaque-to-myocardium signal intensity ratio (PMR).

Results During the follow-up period (median 55 months), coronary events were observed in 55 patients. Receiver-operating characteristic curve analysis identified a PMR of 1.4 as the optimal cutoff for predicting prognosis. Multivariate Cox regression analysis identified the presence of plaques with PMRs $\geq$1.4 as the significant independent predictor of coronary events (hazard ratio: 3.96; 95% confidence interval: 1.92 to 8.17; $p < 0.001$) compared with the presence of CAD (hazard ratio: 3.56; 95% confidence interval: 1.76 to 7.20; $p < 0.001$) and other traditional risk factors. Among the 4 groups based on PMR cutoff and the presence of CAD, coronary event–free survival was lowest in the group with PMRs $\geq$1.4 and CAD and highest in the group with PMRs $<$1.4 but no CAD. Importantly, the group with PMRs $\geq$1.4 and no CAD had an intermediate rate of coronary events, similar to the group with PMRs $<$1.4 and CAD.

Conclusions HIPs identified in a noninvasive, quantitative manner are significantly associated with coronary events and may thus represent a novel predictive factor. (J Am Coll Cardiol 2014;63:989–99) © 2014 by the American College of Cardiology Foundation

Recently, T1-weighted imaging (T1WI) of coronary plaques with or without contrast enhancement using cardiac magnetic resonance (CMR) has been successfully demonstrated (1–4). Because magnetic resonance (MR) imaging generates images without ionizing radiation, it can be repeated sequentially over time. Moreover, MR imaging allows the characterization of plaque composition in addition to morphologic evaluation (5). We have previously shown that the presence of coronary high-intensity plaques (HIPs) detected by noncontrast T1WI is associated with positive coronary artery remodeling, low density on computed tomographic angiography (CTA), and ultrasound attenuation (6). In addition, HIPs can be uniquely assessed using the plaque-to-myocardium signal intensity ratio (PMR) (6). Although our previous findings suggest that coronary HIPs may represent vulnerable lesions, there have been no studies evaluating the relationship between HIPs and subsequent coronary events. Therefore, we designed a prospective study

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Manuscript received August 2, 2013; revised manuscript received November 8, 2013, accepted November 26, 2013.

Abbreviations and Acronyms

ACS = acute coronary syndrome(s)
CAD = coronary artery disease
CI = confidence interval
CMR = cardiac magnetic resonance
CTA = computed tomographic angiography
cTnT = cardiac troponin T
HIP = high-intensity plaque
MI = myocardial infarction
MR = magnetic resonance
PCI = percutaneous coronary intervention
PMR = plaque-to-myocardium signal intensity ratio
ROC = receiver-operating characteristic
T1WI = T1-weighted imaging
UAP = unstable angina pectoris

to determine the prognostic significance of HIPs and to identify the optimal PMR cutoff value for predicting coronary events.

Methods

Patients. Between December 2006 and September 2010, a total of 650 consecutive patients with suspected or known coronary artery disease (CAD) were initially screened with CTA and then underwent CMR examinations. Proven CAD was defined as: 1) a history of myocardial infarction (MI) or percutaneous coronary intervention (PCI); 2) ischemia-proven angina pectoris or silent myocardial ischemia diagnosed with stress myocardial scintigraphy; or 3) coronary arteriography–proven coronary artery stenosis ≥50%. We excluded patients with acute MIs (n = 13), unstable angina pectoris (UAP) (n = 7), left ventricular dysfunction (ejection fraction <40%) (n = 4), scheduled coronary artery bypass grafting (n = 1) or PCI (n = 29), and CMR images of poor quality (n = 28). Thus, 82 patients were excluded, and a total of 568 patients (mean age 62 ± 10 years; 435 men, 133 women) were ultimately enrolled in this study. This study was approved by the institutional review board of the National Cerebral and Cardiovascular Center and the ethics committee of Shin-Koga Hospital.

Coronary CTA. Coronary CTA was performed using a LightSpeed VCT (GE Healthcare, Milwaukee, Wisconsin). Computed tomographic procedures used in this study have been described previously (6).

CMR coronary plaque imaging. CMR imaging consisted of MR angiography and T1WI of plaque using a commercially available 1.5-T MR imager (Intera, Philips Medical Systems, Best, the Netherlands) with 5-element cardiac coils. The procedures used to acquire MR images in this study have been previously described (6). Briefly, coronary plaque images were obtained using a 3-dimensional T1-weighted turbo field echo sequence with inversion recovery (inversion time delay 500 ms) and fat suppression (repetition time 4.7 ms, echo time 1.37 ms, flip angle 20°, sensitivity encoding factor 2.5, number of signals acquired 2, navigator gating window ±1.5 to 2.5 mm, field of view 300 × 270 × 112 mm, acquisition matrices 224 × 200, acquisition slice number 70, reconstruction matrices 512 × 512, reconstruction slice number 140, acquired spatial resolution 1.34 × 1.35 × 1.60 mm, reconstructed to 0.59 × 0.53 × 0.80 mm). The mean acquisition time was 15 ± 3 min for plaque imaging. The average navigator efficiency was 50.5%.

Plaque analysis on CMR. On CMR images, the coronary vascular tree was subdivided into 8 segments (3). For segment identification, segments were pre-defined according to the distance from the vessel origin. The right coronary artery was analyzed in 3 segments (segments 1, 2, and 3). The left coronary artery was analyzed as the left main, left anterior descending (segments 6 and 7), and circumflex (segments 11 and 13) arteries. To confirm that the location of an observed HIP (Fig. 1A) corresponded to the presence of a coronary plaque, we used both cross-sectional (Fig. 1B) and curved multiplanar reformation computed tomographic angiographic images. In addition, for plaque detection, we used coregistration images (Fig. 1C) to facilitate confirmation of the anatomical position of high-intensity lesions on T1-weighted images (Fig. 1A) and the coronary vessel on MR angiography (Fig. 1D) using commercially available software (Virtual Place Raijin workstation, AZE, Tokyo, Japan).

The methods used to evaluate plaque images have been described previously (6). Briefly, an experienced technician and a cardiologist both blinded to patient data used the T1-weighted images to calculate the PMR, defined as the signal intensity of the coronary plaque divided by that of nearby left ventricular myocardium, measured using a free-hand region of interest on a standard console of the clinical MR system. We used left ventricular myocardium located the same distance from the surface coil as the plaque to determine plaque signal intensity. To avoid abnormal myocardial T1 measurements, we did not use areas of MI for reference. The highest signal intensity detected in each plaque was considered the PMR value for that plaque in segment-based analysis. In patient-based analysis, the highest PMR among the coronary plaques was assigned to be the PMR for that subject.

Intraclass correlation coefficients with 95% confidence intervals (CIs) were calculated to assess intrareader and interreader agreement for PMR. The intrareader intraclass correlation coefficient was 0.94 (95% CI: 0.80 to 0.98). The inter-reader intraclass correlation coefficient was 0.88 (95% CI: 0.73 to 0.95). All correlation coefficients for PMR were >0.8, with narrow CIs, indicating good intraobserver and interobserver agreement.

Follow-up study. After CMR data were obtained, study patients were followed at 3, 6, and 12 months and annually thereafter until the occurrence of 1 of the following coronary events: cardiac death, nonfatal ST-segment elevation MI, high-sensitivity cardiac troponin T (cTnT)–positive UAP or non–ST-segment elevation MI, or ischemia-driven PCI due to progressive angina pectoris. Cardiac death was defined as sudden death and death caused by acute MI or ventricular arrhythmias. Elevation of cTnT was defined as more than 2 times the upper limit of the normal range (0.010 ng/ml). Myocardial ischemia was diagnosed using stress myocardial scintigraphy before PCI. PCI-related restenosis and PCI