Assessment of Coronary Plaque Progression in Coronary Computed Tomography Angiography Using a Semiquantitative Score

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OBJECTIVES We sought to describe the progression of coronary atherosclerotic plaque over time by computed tomography (CT) angiography stratified by plaque composition and its association with cardiovascular risk profiles.

BACKGROUND Data on the progression of atherosclerosis stratified by plaque composition with the use of noninvasive assessment by CT are limited and hampered by high measurement variability.

METHODS This analysis included patients who presented with acute chest pain to the emergency department but initially showed no evidence of acute coronary syndromes. All patients underwent contrast-enhanced 64-slice CT at baseline and after 2 years with the use of a similar protocol. CT datasets were coregistered and assessed for the presence of calcified and noncalcified plaque at 1 mm cross sections of the proximal 40 mm of each major coronary artery. Plaque progression over time and its association with risk factors were determined. Measurement reproducibility and correlation to plaque volume was performed in a subset of patients.

RESULTS We included 69 patients (mean age 55 ± 12 years, 59% male patients) and compared 8,311 coregistered cross sections at baseline and follow-up. At baseline, any plaque, calcified plaque, and noncalcified were detected in 12.5%, 10.1%, and 2.4% of cross sections per patient, respectively. There was significant progression in the mean number of cross sections containing any plaque (16.5 ± 25.3 vs. 18.6 ± 25.5, p = 0.01) and noncalcified plaque (3.1 ± 5.8 vs. 4.4 ± 7.0, p = 0.04) but not calcified plaque (13.3 ± 23.1 vs. 14.2 ± 22.0, p = 0.2). In longitudinal regression analysis, the presence of baseline plaque, number of cardiovascular risk factors, and smoking were independently associated with plaque progression after adjustment for age, sex, and follow-up time interval. The semiquantitative score based on cross sections correlated closely with plaque volume progression (r = 0.75, p < 0.0001) and demonstrated an excellent intraobserver and interobserver agreement (κ = 0.95 and κ = 0.93, respectively).

CONCLUSIONS Coronary plaque burden of patients with acute chest pain significantly increases during the course of 2 years. Progression over time is dependent on plaque composition and cardiovascular risk profile. Larger studies are needed to confirm these results and to determine the effect of medical treatment on progression. (J Am Coll Cardiol Img 2009;2:1262–70) © 2009 by the American College of Cardiology Foundation
Serial assessment of coronary plaque burden has contributed to the understanding of the natural history and pathophysiology of coronary artery disease (CAD) and is a surrogate end point for the evaluation of novel cardiovascular therapeutics (1–8). Invasive modalities such as intravascular ultrasound (IVUS) and serial selective coronary angiography are considered gold-standard methods to measure the progression of atherosclerotic plaque and stenoses over time (4). However, these modalities are limited by their invasive nature and by the specific characteristics they are able to measure. Noninvasively, repeated measurements of coronary artery calcium (CAC) by electron-beam or multidetector computed tomography (CT) have been used to assess changes in CAC burden. However, CAC represents only 1 component of atherosclerotic plaque, and follow-up studies (2,9–12) of CAC in which the authors assessed the role of both medical therapies and cardiovascular risk factors have led to contradictory results. More recently, contrast-enhanced coronary multidetector CT has been established as a robust and reliable modality to noninvasively detect the presence, extent, and composition of coronary plaque (13,14). However, the few studies available (15,16) suggest a high measurement variability of quantitative assessment of plaque area and volume data.

In the present study, we determined the intraobserver and interobserver variability of a new semiquantitative method to assess the presence, extent, and composition of atherosclerotic plaque as detected by 64-slice coronary CT angiography. This method was used to assess changes in atherosclerotic plaque burden during the course of 2 years in a cohort of patients with acute chest pain. In addition, we evaluated measurement variability of our semiquantitative score based on cross sections and its correlation to plaque volume measurements. Finally, we determined whether changes in atherosclerotic plaque burden were independently associated with traditional cardiovascular risk profiles and correlated this new score with change in plaque volume in a subset of patients.

**METHODS**

**Patients.** Patients were prospectively enrolled from the ROMICAT (Rule Out Myocardial Infarction using Computer Assisted Tomography) trial, a prospective, observational cohort study of coronary CT angiography in patients with acute chest pain but an inconclusive initial evaluation (negative cardiac enzymes, nondiagnostic electrocardiography) in the emergency department (17).

The present study was performed in consecutive subjects who agreed to participate in a 2-year follow-up. These patients were contacted by phone, and the return visit included a structured clinical interview. Subjects with a creatinine clearance of <50 ml/min or atrial fibrillation were excluded. All other subjects underwent repeated contrast-enhanced coronary CT scanning (n = 69). The study was approved by the institutional review board of the Massachusetts General Hospital, and all subjects provided written informed consent.

**Coronary CT acquisition.** Baseline and follow-up cardiac CT scans were performed with the use of 64-slice scanner technology (Sensation 64, Siemens Medical Solutions, Forchheim, Germany) and identical acquisition protocols as detailed previously (17). Axial CT images were reconstructed with a slice thickness of 0.75 mm and increments of 0.4 mm with retrospective electrocardiogram gating.

**Coronary CT image analysis.** Coronary reconstructions blinded to patient name and study date were transferred to an offline workstation and curved multiplanar reconstructions generated (Circulation, Leonardo, Siemens Medical Solutions). The extent of atherosclerotic plaque burden at both baseline and follow-up was assessed for the entire left main coronary artery (LM) and the proximal 40 mm of the left anterior descending (LAD), left circumflex (LCX), and right (RCA) coronary artery on 1-mm thick cross sections reconstructed in 1-mm increments without gaps or overlaps (Fig. 1). The proximal coronary tree was selected for analysis because these segments contain the culprit lesions in the majority of acute coronary syndrome presentations and typically have greater image quality on contrast-enhanced CT than distal segments (18,19).

For the LCX, the larger of the true circumflex and the obtuse marginal artery was analyzed. To ensure correct coregistration, the first cross section analyzed in any vessel was immediately distal to either the aorta (in the case of the LM and RCA) or the bifurcation of the LAD and LCX (for LAD and LCX). The centerline of the artery was used to advance in 1-mm increments distally to obtain the second and all subsequent cross sections.

Reconstructed arteries and cross sections were first analyzed for image quality by 2 experienced

**ABBREVIATIONS AND ACRONYMS**

- **CAC** = coronary artery calcium
- **CAD** = coronary artery disease
- **CI** = confidence interval
- **CT** = computed tomography
- **CVRF** = cardiovascular risk factors
- **FRS** = Framingham Risk Score
- **IVUS** = intravascular ultrasound
- **LAD** = left anterior descending coronary artery
- **LCX** = left circumflex coronary artery
- **LM** = left main coronary artery
- **RCA** = right coronary artery
observers and graded as evaluable or nonevaluable. An artery or cross section was determined nonevaluable when either motion or poor contrast-to-noise ratio rendered the detection of plaque in the artery impossible. Any cross section deemed nonevaluable either at baseline or follow-up was excluded from analysis.

An experienced reader, blinded to time of scanning (baseline/follow-up), determined the presence of calcified or noncalcified plaque in all evaluable cross sections. Calcified plaque was defined by any structure distinct from the vessel lumen within the artery wall with a CT attenuation of $>130$ Hounsfield units (HU). The presence of any calcification within the corresponding cross section rendered the cross section as calcified. Noncalcified plaque was defined by a structure assigned to the coronary artery wall with CT attenuation above the surrounding tissue but below that of the contrast enhanced lumen without any calcified plaque being present (20).

Interobserver and intraobserver variability for plaque detection were assessed in 15 randomly selected subjects at baseline and follow-up by 2 independent observers blinded to the patient identity and scan date and with a lag period of 2 weeks between the intraobserver readings.

To compare volumetric plaque progression with the semiquantitative score, only patients who had plaque at baseline were eligible ($n = 38$). In addition, we limited our analysis to arteries with excellent image quality because measurements of plaque volume are more likely to be affected by decreased image quality than the newly defined score; Pfederer et al. (21) demonstrated significantly increased interobserver variability for quantification of coronary plaque in cases with poor image quality. As a result, we measured plaque volume (in mm$^3$) at baseline and follow-up in 34 vessels (18 LAD, 10 LCX, and 6 RCA in 24 patients) by using automated software on an offline workstation (SUREPlaque, Vitrea 2, Vital Images, Plymouth, Minnesota). The outer vessel boundary and inner luminal boundary of the proximal 40 mm of the selected coronary artery initially were automatically traced and subsequently manually adjusted in a cross-sectional view. Pixels with attenuation between $+1,300$ and $-100$ HU within the area between outer vessel boundary and inner luminal boundary were defined as plaque.

**Clinical covariates.** At baseline, we collected information on cardiovascular risk profile for all study...
participants. History of CAD was defined by previous symptomatic CAD treated by medication or coronary revascularization (stent placement or coronary bypass grafting). Measurement of blood pressure, serum lipids, and fasting blood glucose was obtained during index presentation. Hypertension was defined by a systolic blood pressure of $\geq 140$ mm Hg or diastolic pressure of $\geq 90$ mm Hg or current antihypertensive treatment. Hyperlipidemia was defined by a total cholesterol $\geq 200$ mg/dl or treatment with lipid-lowering medication and diabetes by fasting blood glucose $\geq 126$ mg/dl or treatment with hypoglycemic medication. Smoking was defined by current or previous daily cigarette use. Family history of CAD was defined as the occurrence of myocardial infarction in a first-degree relative $<55$ years of age for men and $<65$ years of age for women. Statin medication was defined as ongoing statin treatment at baseline. The Framingham Risk Score (FRS) was calculated for each patient by use of the established regression model (22).

**Statistical analysis.** Continuous measures were summarized by mean $\pm$ SD and categorical by percentage (counts) unless otherwise specified. Accordingly, the Wilcoxon signed rank test, paired $t$ test, and the Fisher exact test were used to assess for differences within continuous and categorical variables. Evaluation of interobserver and intraobserver agreement was performed by Kappa statistic.

Linear regression was used to determine the amount of plaque volume contained in a single cross section including the 95% confidence intervals (CIs). Absolute and relative change in plaque burden by use of the semiquantitative score and the volumetric approach were determined with a Pearson correlation coefficient ($r$).

To estimate the mean plaque rate change during the 2-year follow-up interval after adjusting for the known cardiovascular risk factors (CVRF), longitudinal linear regression models were used, which handled the correlated outcomes within persons measured on the baseline and follow-up by the generalized estimating equations approach with identity link function. Further, the top quartile of plaque progression was used to identify subjects who progressed rapidly and were compared with demographics, statin use, and return visits to the emergency department with the remaining cohort.

To balance specificity and sensitivity to detect progression, we prospectively determined that the number of cross sections containing plaque per patient had to increase by at least 2 to represent progression. To maintain sensitivity, we performed measurements in 1-mm increments. To maintain specificity, an increase of at least 2 was required. All performed tests were 2-sided, and a value of $p < 0.05$ was considered as statistically significant.

**RESULTS**

**Patients.** Baseline demographics for the 69 patients are presented in Table 1. The mean age of patients returning was $55 \pm 12$ years, 59% were men, and 10 patients had a history of CAD (14.5%). The median FRS in the cohort was 9 (interquartile range 4.5 to 11.4).

**Image quality.** Heart rate during the scan was not different between baseline and follow-up (63.0 $\pm$ 7.3 beats/min vs. 62.7 $\pm$ 7.5 beats/min, $p = 0.63$, respectively). There were 11 (4.0%) of 276 arteries and 640 (7.0%) of 9,199 cross sections that were not evaluable at baseline, and of these, 10 (90.9%) of 11 arteries and 513 (80.2%) of 640 cross sections also were not evaluable at follow-up. There were an additional 2 (0.7%) of 276 arteries and 248 (2.7%) of 9,199 cross sections not evaluable at follow-up. Hence, among all patients a total of 13 (4.7%) of 276 arteries and 888 of (9.7%) 9,199 cross sections were excluded from analysis as the result of image quality (motion or poor contrast-to-noise ratio).

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<th>Table 1. Baseline Demographics of 69 Subjects Who Underwent Repeat 64-Slice Coronary CT Angiography</th>
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Values are presented as absolute numbers with percentages or mean $\pm$ SD. Framingham Risk Score is presented as median (interquartile range). History of CAD = documented history of symptomatic CAD. CAD = coronary artery disease; CT = computed tomography.
Progression of coronary atherosclerotic plaque burden expressed as a change in the percentage of cross sections containing plaque between baseline and follow-up as detected by 64-slice coronary computed tomography stratified by plaque composition. Among 69 subjects, the mean number of cross sections containing any plaque increased by 12.7% (16.5 ± 25.3 vs. 18.6 ± 25.5, p = 0.01) during a period of 24 ± 3 months. Stratification by plaque composition revealed a significant 41.9% increase in noncalcified plaque (3.1 ± 5.8 vs. 4.4 ± 7.0 cross sections containing noncalcified plaque, p = 0.04) but no significant increase in calcified plaque (13.3 ± 23.1 vs. 14.2 ± 22.0 cross sections containing calcified plaque, p = 0.2).

Reproducibility of plaque assessment. In a subset of 15 randomly selected patients at baseline and follow-up (n = 4,057 cross sections) the intraobserver and interobserver agreement for the detection of any plaque per cross section was excellent (κ = 0.95, 95% CI: 0.94 to 0.97 and κ = 0.93, 95% CI: 0.92 to 0.95, respectively). Plaque type-specific analysis and intraobserver and interobserver agreement were excellent for the detection of calcified (κ = 0.96, 95% CI: 0.95 to 0.97 and κ = 0.97, 95% CI: 0.96 to 0.98, respectively) and very good for the detection of noncalcified (κ = 0.76, 95% CI: 0.68 to 0.83 and κ = 0.73, 95% CI: 0.65 to 0.81, respectively) plaque.

Atherosclerotic plaque burden at baseline. At baseline, on average 16.5 ± 25.3 (12.5%) cross sections contained any atherosclerotic plaque per patient (Table 2). Calcified plaque was detected 5 times more frequently than noncalcified plaque (13.3 ± 23.1 [10.1%] and 3.1 ± 5.8 [2.4%], respectively).

Change of atherosclerotic plaque burden over time. We observed a significant 12.7% increase in the mean number of cross sections containing any plaque (16.5 ± 25.3 vs. 18.6 ± 25.5, p = 0.01) (Table 2, Fig. 2). When stratified by plaque composition, there was a significant 41.9% increase in noncalcified plaque (3.1 ± 5.8 vs. 4.4 ± 7.0, p = 0.04) but no significant increase in mean number of cross sections containing calcified plaque (13.3 ± 23.1 vs. 14.2 ± 22.0, p = 0.2).

| Table 2. Coronary Atherosclerotic Plaque Burden at Baseline and 2-Year Follow-Up per Subject and Each Coronary Artery Defined as Cross Sections in Whom Plaque Was Detected |
|------------------|------------------|------------------|------------------|------------------|
|                  | Number of Cross Sections With Plaque at Baseline | Number of Cross Sections With Plaque at Follow-Up | Absolute and Relative Plaque Progression | p Value |
| Any plaque       |                  |                  |                  |                  |
| Per subject      | 16.5 ± 25.3 (12.5) | 18.6 ± 25.5 (14.1) | 2.1 (12.7) | 0.01 |
| LM               | 1.5 ± 3.0 (11.6) | 2.2 ± 3.7 (16.6) | 0.6 (40.0) | 0.005 |
| LAD              | 8.0 ± 11.5 (20.0) | 8.2 ± 10.7 (20.5) | 0.2 (2.5) | 0.7 |
| LCX              | 3.7 ± 8.1 (9.3) | 4.6 ± 9.1 (11.4) | 0.8 (24.3) | 0.001 |
| RCA              | 3.2 ± 7.0 (8.1) | 3.7 ± 7.0 (9.1) | 0.4 (15.6) | 0.5 |
| Calcified plaque |                  |                  |                  |                  |
| Per subject      | 13.3 ± 23.1 (10.1) | 14.2 ± 22.0 (10.8) | 0.9 (6.8) | 0.2 |
| LM               | 1.1 ± 2.6 (8.1) | 1.3 ± 2.8 (11) | 0.2 (18.2) | 0.01 |
| LAD              | 6.9 ± 10.9 (17.2) | 6.9 ± 10.4 (17.2) | 0 (0) | 0.9 |
| LCX              | 3.1 ± 7.3 (7.7) | 3.5 ± 7.7 (8.7) | 0.4 (12.9) | 0.005 |
| RCA              | 2.8 ± 6.4 (7.0) | 3.1 ± 6.2 (7.9) | 0.7 (10.7) | 0.009 |
| Noncalcified plaque |                  |                  |                  |                  |
| Per subject      | 3.1 ± 5.8 (2.4) | 4.4 ± 7.0 (3.4) | 1.3 (41.9) | 0.04 |
| LM               | 0.5 ± 1.6 (4.3) | 0.9 ± 2.1 (6.4) | 0.4 (80.0) | 0.07 |
| LAD              | 1.3 ± 2.8 (3.3) | 1.6 ± 3.4 (4.0) | 0.3 (23.1) | 0.4 |
| LCX              | 0.8 ± 2.5 (1.9) | 1.2 ± 3.3 (3.1) | 0.9 (112.5) | 0.03 |
| RCA              | 0.6 ± 2.4 (1.6) | 0.9 ± 2.2 (2.1) | 0.2 (33.3) | 0.5 |

Values are presented as mean ± SD (%) or mean (%).
LAD = left anterior descending coronary artery; LCX = left circumflex coronary artery; LM = left main coronary artery; RCA = right coronary artery.
Overall, plaque progression (defined as ≥2 cross sections containing plaque) occurred in 26 (37.7%) of 69 subjects, no change was observed in 43 (62.3%) of 69 subjects, and none of the subjects, 0 (0%) of 69, demonstrated plaque regression. Among patients in whom plaque was detected on the baseline scan, plaque progression occurred in 20 (52.6%) of 38, whereas no change was observed in the remaining 18 (47.4%) of 38 patients.

Correlation of the semiquantitative score to progression of actual plaque volume. In a subset of 34 vessels, on average 9 ± 7 cross sections of plaque with a plaque volume of 100 ± 77 mm³ at baseline and on average 11 ± 8 cross sections of plaque with a plaque volume of 125 ± 91 mm³ at follow-up were detected. One cross section contained an average plaque volume of 7.6 mm³ (95% CI: 5.8 mm³ to 9.5 mm³). Absolute and relative change in the semiquantitative score were strongly correlated with absolute and relative change in plaque volume (r = 0.75, p < 0.0001 and r = 0.79, p < 0.0001, respectively) (Fig. 3).

Change of atherosclerotic plaque burden over time and its association with cardiovascular risk factors and demographics. In univariate longitudinal regression models age, male sex, hypertension, hyperlipidemia, history of CAD, number of CVRFs, FRS, the presence of baseline plaque, and baseline statin medication were significantly associated with progression of any atherosclerotic plaque (Fig. 4).

In models adjusted for age, sex, and the follow-up time interval, the presence of baseline plaque, number of CVRFs, smoking, and baseline statin medication were associated with increase in plaque during the follow-up period (Fig. 5).

Subjects who were in the highest quartile of plaque progression (n = 17) did not differ with respect to age, sex, and statin medication (p = 0.63, p = 0.39, and p = 0.38, respectively) from the remaining cohort. In contrast, subjects with rapid progression were more likely to return to the emergency department with recurrent chest pain as compared with the remaining cohort (29.4% vs. 7.7%, p = 0.03).

**DISCUSSION**

In this study, we demonstrate a significant increase in coronary plaque burden during a 2-year period (12.7%, p = 0.01) among patients with acute chest pain, but without acute coronary syndromes, by using a highly reproducible semiquantitative assessment of coronary plaque burden (κ = 0.95 and κ = 0.93 for intraobserver and interobserver agreement, respectively). Our results further indicate that there are differences in the rate of progression according to plaque composition because we found no significant progression for calcified plaque whereas non-calcified plaque progressed significantly over time (41.9%, p = 0.04). Progression of plaque was significantly associated with the presence of baseline plaque, smoking, statin use, and number of cardiovascular risk factors in adjusted analysis. Furthermore, in a subset of vessels, we demonstrate a robust correlation of the absolute and relative change of the semiquantitative score to progression of actual plaque volume (r ≥ 0.75, p < 0.0001 for both).

Although feasibility of quantitative measurement of coronary plaque volume by 16- and 64-slice CT with the use of methodology similar to IVUS has been previously described in selected patients with exceptional image quality, the authors of these studies (15,16) found substantial interobserver variability for the assessment of plaque volume between 16% and 37%. The lack of agreement has been related to low contrast resolution of CT and the resulting difficulty...
to correctly delineate the boundaries of smaller non-calcified plaques, and it further indicates the limited utility of this method for progression studies. As a result, many investigators (23–25) have returned to using a qualitative description of plaque burden most often stratified by coronary segments.

In this study, we introduced a semiquantitative technique with excellent observer reliability for both calcified and noncalcified plaque that is based on the detection of plaque presence in consecutive cross sections. This technique rendered a low interobserver variability of 0.2%, which is a prerequisite to assess changes in plaque burden over time. Furthermore, we found a good correlation between absolute and relative change of the new semiquantitative score with volumetric plaque progression (9 ± 7 to 11 ± 8 cross sections containing plaque compared with 100 ± 77 mm$^3$ to 125 ± 91 mm$^3$ at baseline and follow-up, respectively, $r = 0.75, p < 0.0001$ for both). The high concordance indicates that the semiquantitative approach provides a good estimate of volumetric progression and that the differences as a result of cross-sectional plaque progression (e.g., positive remodeling) may be limited. Although these initial results are encouraging, they warrant further confirmation in larger studies, optimally with the use of IVUS and a detailed quantitative assessment of remodeling index.

Our results suggest that the rate of progression in patients presenting to the emergency department with acute chest pain over the course of 2 years is 12.7% for any plaque. Although we observed a large relative and significant increase in noncalcified plaque at 2-year follow-up (3.1 ± 5.8 baseline vs. 4.4 ± 7.0 follow-up, $p = 0.04$), the absolute change was similar between calcified and noncalcified plaque. This observation is in contrast to previous CT studies (3,9–12) on the progression of CAC in which the authors reported progression as high as 40% per year even in asymptomatic subjects. However, it is consistent with the IVUS study of Achenbach et al. (20), in which they suggest that the plaques may undergo only minimal changes over time (<1% per year atheroma volume measured by IVUS). The discrepancy may be explained by the fact that most of CAC progression studies (22,26) have relied on CT imaging acquisition techniques that have been shown to have significant measurement variability.

In our study, the negative association between plaque progression and diabetes is likely a reflection of the small number of diabetic patients within the cohort ($n = 4$). Similarly, the finding that current statin treatment was associated with plaque progression can be attributed to confounding by history of CAD. However, our results suggest that subjects who had the greatest rates of plaque progression (top quartile) were re-evaluated for recurrent chest pain more frequently during follow-up as compared with subjects in the bottom quartile of progression. Strengths and limitations. The baseline and follow-up CT scans were performed on the same scanner and adhered to a standard protocol. A further strength is the standardized assessment of plaque, including assessment of intraobserver and interobserver variability for both calcified and noncalcified plaque. Furthermore, the study used a longitudinal regression model that enabled an assessment of progression accounting for baseline plaque burden and used prospectively collected information on cardiovascular risk factors.

Our assessment is limited to the LM and the first 40 mm of the main coronary arteries. However, capturing proximal plaque may be most relevant because the majority of clinical events arise from these plaques (18). Although we used dedicated coronary evaluation software, which permits the automated reconstruction of cross-sectional images,
the evaluation of each cross section remains time consuming (15 to 20 min per patient). Further improvements in coregistration and documentation of assessments are necessary to enhance practicality. In addition, our assessment does not capture cross-sectional plaque extension such as area growth or remodeling, which are important aspects of the progression of individual plaques. However, we found a robust correlation between volumetric progression and longitudinal semiquantitative assessment (Pearson’s correlation coefficient 0.75; p < 0.0001 for both absolute and relative change).

Finally, the present study describes the progression of atherosclerotic plaque stratified as calcified and noncalcified plaque. We omitted the category of mixed plaque because plaques observed as calcified on CT usually also contain noncalcified (fibrous or lipid rich) components, which are not visualized on CT because of the blooming effect of calcification (27). Moreover, in the current analysis, we determined plaque progression on a cross section rather than on a plaque basis.

Clinical implications. A reliable noninvasive method to serially evaluate both calcified and noncalcified plaque provides a unique opportunity to validate plaque progression as a surrogate marker for the assessment of cardiovascular risk and most importantly for the effect of medical therapies for cardiovascular disease. The ability to detect progression of noncalcified plaque warrants further assessment and validation, especially as a potential surrogate marker for the effects of medical therapy.

CONCLUSIONS

Coronary plaque burden of patients with acute chest pain significantly increases during the course of 2 years, but rate of progression is dependent on plaque composition and may be greater for noncalcified compared with calcified plaque. Progression is further associated with cardiovascular risk profile at baseline. Larger studies are needed to confirm these results and to determine effect of medical treatment on progression.

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REFERENCES


Figure 5. Multivariate Adjusted Predictors of Plaque Progression

Estimated effect sizes of covariates in longitudinal regression models adjusted for age, sex, and the follow-up time interval. The forest plot displays estimated effect sizes of regression coefficients with 95% confidence intervals (x-axis). Covariates associated with a significant increase in plaque at 2 years were smoking, the presence of baseline plaque, and number of cardiovascular risk factors as a continuous (cont.) variable. *Years of age, as compared to patients younger than 45 years; **number of positive cardiovascular risk factors (hyper-tension, hyperlipidemia, diabetes, smoking, and family history of coronary artery disease, as compared to patients with no CVRF). Abbreviations as in Figure 4.


Key Words: atherosclerosis • computed tomography • coronary artery disease • risk factors • progression.