Computed Tomography Coronary Angiography in Patients With Acute Myocardial Infarction Without Significant Coronary Stenosis

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Background—It is known that a significant number of patients experiencing an acute myocardial infarction have normal coronary arteries or nonsignificant coronary disease at coronary angiography (CA). Computed tomography coronary angiography (CTCA) can identify the presence of plaques, even in the absence of significant coronary stenosis. This study evaluated the role of 64-slice CTCA in detecting and characterizing coronary atherosclerosis in these patients.

Methods and Results—Consecutive patients with documented acute myocardial infarction but without significant coronary stenosis at CA underwent late gadolinium-enhanced magnetic resonance and CTCA. Only the 50 patients with an area of myocardial infarction identified by late gadolinium-enhanced magnetic resonance were included in the study. All of the coronary segments were assessed for the presence of plaques. CTCA identified 101 plaques against the 41 identified by CA: 61 (60.4%) located in infarct-related arteries (IRAs) and 40 (39.6%) in non-IRAs. In the IRAs, 22 plaques were noncalcified, 17 mixed, and 22 calcified; in the non-IRAs, 5 plaques were noncalcified, 8 mixed, and 27 calcified (P=0.005). Mean plaque area was greater in the IRAs than in the non-IRAs (6.1±5.4 mm² versus 4.2±2.1 mm²; P=0.03); there was no significant difference in mean percentage stenosis (33.5%±14.6 versus 31.7%±12.2; P=0.59), but the mean remodeling index was significantly different (1.25±0.41 versus 1.08±0.21; P=0.01).

Conclusions—CTCA detects coronary plaques in nonstenotic coronary arteries that are underestimated by CA, and identifies a different distribution of plaque types in IRAs and non-IRAs. It may therefore be valuable for diagnosing coronary atherosclerosis in acute myocardial infarction patients without significant coronary stenosis. (Circulation. 2012;126:3000-3007.)

Key Words: acute myocardial infarction ■ magnetic resonance imaging ■ multidetector computed tomography

Acute myocardial infarction (AMI) is usually a result of coronary artery thrombosis, complicating atherosclerotic coronary plaque in the presence of obstructive coronary artery disease. The absence of angiographic evidence of significant coronary stenosis may challenge a diagnosis of AMI, but coronary atherosclerosis may be present even in angiographically normal coronary arteries because their outward remodeling can take place in the case of mild atherosclerotic plaque not affecting the coronary lumen, and an AMI may occur because of the disruption of only mildly stenotic vulnerable plaques that are undetectable by conventional coronary angiography.¹⁻² It is known that the vulnerable plaques that most frequently lead to thrombotic complications are rich in lipids and have a thin fibrous cap, which may also be found in angiographically normal coronary arteries.³ It has been reported that normal coronary angiography findings can be seen in 9% to 31% of the women and 4% to 14% of the men experiencing an AMI.⁴⁻⁶ and, although coronary angiography is the reference method for assessing coronary artery disease, the results of intravascular ultrasonography and pathological studies indicate that it underestimates the extent of coronary atherosclerosis, especially in the case of mild disease.⁷⁻⁹

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Computed tomography coronary angiography (CTCA) is an emerging imaging technique that allows the noninvasive detection of coronary artery stenosis and atherosclerotic plaques. In comparison with intravascular ultrasonography, it
reliably quantifies plaque area in vivo, and assesses the morphology and composition of atherosclerotic plaques on the basis of attenuation values in patients with stable coronary artery disease and acute coronary syndrome.10–13

Late gadolinium-enhanced cardiac magnetic resonance (LGE-CMR) is an imaging technique that provides detailed information about the characteristics of myocardial tissue and detects myocardial fibrosis with a high degree of diagnostic accuracy.14–16 It has become the gold standard for the in vivo detection of myocardial infarction.17

The aim of this study was to evaluate the presence and morphological characteristics of coronary atherosclerosis by means of CTCA in patients with AMI documented by means of LGE-CMR but without any significant coronary stenosis at coronary angiography.

Patients and Methods
During the study period (January 1, 2009 – December 31, 2010), 2079 patients with AMI were admitted to our institution and underwent coronary angiography. Myocardial infarction was defined as follows: (1) typical chest pain lasting >20 minutes; (2) persistent electrocardiographic changes; and (3) increased cardiac enzymes (troponin I >99th percentile and creatine kinase MB levels more than twice the upper normal limit). A total of 76 patients with AMI did not show any coronary lesion with ≥50% diameter stenosis at coronary angiography.

The study exclusion criteria were as follows: (1) the presence of any coronary stenosis causing a ≥50% reduction in lumen diameter, as evaluated by coronary angiography; (2) a pacemaker or metal device contraindicating CMR; (3) the absence of late enhancement, suggesting myocardial infarction at LGE-CMR; (4) a history of previous myocardial infarction or cardiomyopathy; (5) creatinine clearance <30 mL/min; (6) an allergic reaction after contrast administration during coronary angiography.

Five patients were excluded because of contraindications to CTCA or CMR; the remaining 71 were asked to undergo late gadolinium-enhanced CMR and 64-slice CT within 10 days of coronary angiography. Only the patients showing an area of late enhancement at CMR with a pattern compatible with MI were included in the study, which excluded a further 21 patients. The final study population therefore consisted of 50 prospectively enrolled patients.

The patients’ demographic, ECG, laboratory, and left ventricular function data were recorded. The ejection fraction was measured by 2D echocardiography, if available. In case of incomplete echocardiographic data, the ejection fraction was obtained by means of echocardiography or angiography during the index hospitalization.

All of the patients gave their written informed consent to the study protocol, which was approved by our Institutional Review Board.

Coronary Angiography
Selective conventional coronary angiography was performed using standard techniques (Innova 2000 GE, General Electric, Milwaukee, WI). Standard multiple projections were recorded for the left and right coronary arteries. Left ventriculography was performed in the right oblique projection. All of the coronary angiograms were evaluated by an experienced angiographer. The severity of coronary stenosis was visually estimated, as was the presence of calcifications and subtle changes in lumen contour.

CTCA Data Acquisition
All of the CT examinations were performed using a 64-slice CT scanner (Sensation 64 Cardiac, Siemens, Forchheim, Germany). First, a prospective ECG-triggered unenhanced scan was made using standardized parameters (20 slices per rotation, 1.2 mm detector collimation, gantry rotation time 330 ms, tube voltage 120 kV, tube current 150 mAs) to assess the coronary artery calcium (CAC) score. This was followed by the CT angiographic acquisition using the following parameters: 64 (32×2) slices per rotation, 0.6 mm detector collimation, gantry rotation time 330 ms, effective temporal resolution 165 ms, spatial resolution 0.4 mm³, tube voltage 120 kV. The reconstruction slice thickness and increment were, respectively, 0.75 mm and 0.4 mm. Sublingual nitroglycerine 0.3 mg was administered to all of the patients before the examination, and an intravenous β-blocker (atenolol 5–10 mg) to all of the patients with a heart rate of >65 bpm for whom there was no contraindication. Between 80 and 100 mL of nonionic contrast medium (Iomeron 400, Bracco, Milan, Italy) were administered through the antecubital vein at a flow rate of 4 to 6 mL/s, followed by a 50 mL saline chaser. A bolus tracking technique was used to synchronize the arrival of the contrast in the coronary arteries, and the scan was started once contrast attenuation in a preselected region of interest in the ascending aorta reached a predefined threshold of +100 Hounsfield units (HU). All of the images were acquired during an inspiratory breath hold of approximately 10 to 12 seconds. The estimated radiation dose was 12 mSv.

CTCA Data Analysis
The CTCA data set was analyzed by 2 independent and experienced readers who were unaware of the coronary angiography and CMR findings and used an off-line workstation software package (Leonardo, Siemens Medical Solutions, Forchheim, Germany). CAC was identified as a dense area in the coronary artery whose attenuation exceeded the threshold of 130 HU, and the CAC score was assessed using dedicated software (CaScore, Siemens Medical Solutions, Forchheim, Germany). The overall calcium score for each patient was calculated using the Agatston score algorithm.18

To obtain optimal image quality, angiographic CT datasets of the reconstructed coronary vessels were created for at least 2 phases of the cardiac cycle using a retrospective ECG gating algorithm (1 diastolic cardiac phase usually = 350 ms from the R waves, and 1 end-systolic phase at +275 ms). In the case of motion artifacts, additional reconstructions were made at different times during the R–R interval.

The presence of plaques was assessed using original axial images, multiplanar reconstruction (MPR), and cross-sectional reconstruction. All of the coronary segments were analyzed in accordance with the American Heart Association (AHA) classification,19 and each segment was delimited by identifiable side-branches. The following parameters were considered: plaque localization, plaque type, maximum plaque area, the remodeling index, vessel stenosis, minimal noncalcified plaque attenuation, and the presence/absence of spotty calcifications.

Noncalcified coronary atherosclerotic plaque was defined as any discernible structure that could be assigned to the coronary artery wall, had a CT density that was less than that of the contrast-enhanced coronary lumen and greater than that of the surrounding epicardial fatty tissue, and could be identified in at least 2 independent planes.20 Calcified atherosclerotic plaque was defined as any structure with a density of ≥130 HU that could be assigned to the coronary artery wall, visualized separately from the contrast-enhanced coronary lumen (because it was embedded in noncalcified plaque or its density was greater than that of the contrast-enhanced lumen), and could be identified in at least 2 independent planes.21 The display settings used for the lumen and plaque analyses were manipulated to achieve optimal separation between the vessel lumen, wall, and surrounding tissue and minimize blooming artifacts in the case of calcified plaques.

A cross-sectional image of each coronary segment was created on multiplanar reconstructions perpendicularly to the center-line of the vessel. In the presence of coronary plaque, the outer vessel contour at the point of maximum plaque area was manually traced to measure the vessel area, which was also measured in a coronary segment without any detectable atherosclerosis proximal to the lesion and used as the reference vessel area. The maximum plaque and lumen areas were also manually traced.

The remodeling index was calculated by dividing the vessel area at the plaque site by the reference vessel area. A remodelling index of >1.1 (corresponding to a lesion site vessel area that is 10% larger than the reference segment) was considered positive remodeling.
Plaque attenuation was measured, and the plaques were classified as calcified if the attenuation value was ≥130 HU, noncalcified if it was <130 HU, or mixed if there were areas whose densities were both >130 and <130 HU.

Spotty calcification was defined as a small calcification of <3 mm on multplanar reconstruction, embedded in noncalcified material and 1-sided on cross-sectional images.22

**CMR Data Acquisition and Image Analysis**

All of the CMR studies were acquired using a 1.5T MRI system (Philips Achieva, Philips Medical System, Best, The Netherlands), commercially available cardiac MRI software, vector electrocardiographic triggering, and a dedicated 5-channel phase-array surface coil. After determining the cardiac axes by means of localizers, breath-hold steady-state free-precession cine MRIs were acquired in short axis views from the cardiac base to the apex (10 mm slice thickness without gap), and vertical and horizontal long axis views to assess left ventricular volumes and mass, regional wall motion, and the ejection fraction. The image parameters were as follows: TR 2.9 ms, TE 1.46 ms, flip angle 60, slice thickness 8 mm, matrix 160×256, field of view 320×360 mm; voxel size 1.6 mm/1.6 mm, and 30 phases.

Ten minutes after the intravenous injection of 0.2 mmol/kg of Gadolinium-BOPTA (Multihance, Bracco, Milan, Italy) at 2 mL/s, a breath-hold, T1-weighted, 3-dimensional, inversion-recovery prepared gradient echo sequence was used to depict the myocardial infarct. The imaging parameters were as follows: TR 4.2 ms, TE 1.3 ms, flip angle 15, 10 contiguous partitions, slice thickness 5 mm, matrix 128×256; field of view 350 mm, and in-plane resolution 1.4 mm/1.4 mm. The images were obtained in cardiac short axis view covering the left ventricle from the base to the apex, and in both long axes. The inversion time was selected to null the signal of normal myocardium (typical values 220–300 ms).

All of the MRI studies were analyzed using an off-line workstation (ViewForum, Philips Medical Systems). The LGE images were analyzed by 2 experienced readers for the presence and localization of myocardial infarction, which was defined as a hyperintense area whose signal intensity was >5 standard deviations (SDs) greater than that of the remote myocardium23 and whose subendocardial or transmural distribution was compatible with coronary distribution. Infarct size was expressed as absolute mass. The left ventricle was divided on the basis of the AHA 17-segment model.24

**Infarct-Related Artery Analysis**

For each patient, the infarct-related artery (IRA) was identified on the basis of the myocardial infarction location shown by the LGE-CMR images, and the association between coronary artery distribution and myocardial segments was analyzed on the basis of the AHA recommendations.24 The left main coronary artery was considered part of the left anterior descending coronary artery, and the intermediate branch was considered part of the left circumflex coronary artery.

A subsequent comparison was made of the distribution and characteristics of the coronary plaques located in IRAs and those located in non-IRAs using the following parameters: (1) percentage coronary stenosis; (2) plaque area; (3) the type of plaque (calcified, noncalcified or mixed); (4) the remodeling index; and (5) the presence of spotty calcifications.

**Statistical analysis**

The normally distributed continuous variables were expressed as mean values and SD, and compared using the t test for independent samples; the continuous variables that were not normally distributed were expressed as median values. The quantitative data are given as mean values±SD. The categorical values were expressed as numbers and percentages and compared using the χ2 test. A probability value of <0.05 was considered significant.

The statistical analyses were made using SPSS software, version 12.0 (SPSS Inc, Chicago, IL).

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**Table 1. Patient Characteristics**

<table>
<thead>
<tr>
<th>No. of patients</th>
<th>50</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age±SD, years</td>
<td>59.3±11.7</td>
</tr>
<tr>
<td>Males</td>
<td>20 (40%)</td>
</tr>
<tr>
<td>Females</td>
<td>30 (60%)</td>
</tr>
</tbody>
</table>

**Risk factors**

- Family history: 15 (30%)
- Hypertension: 28 (56%)
- Dyslipidemia: 13 (26%)
- Smoking: 13 (26%)
- Diabetes mellitus: 4 (8%)
- Obesity: 9 (18%)

**Clinical presentation**

- NSTEMI: 34 (68%)
- STEMI: 16 (32%)

**Mean peak creatine kinase MB level (ng/ml)**

- NSTEMI: 38.2±4.3
- STEMI: 7.4±9.6

**Mean peak troponin I level (ng/ml)**

<table>
<thead>
<tr>
<th>Location of AMI at LGE-CMR</th>
<th>Mean ejection fraction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anterior</td>
<td>44.7%±19.5%</td>
</tr>
<tr>
<td>Inferior</td>
<td>29 (58%)</td>
</tr>
<tr>
<td>Lateral</td>
<td>13 (26%)</td>
</tr>
<tr>
<td>Inferior</td>
<td>8 (16%)</td>
</tr>
</tbody>
</table>

Abbreviations: AMI, acute myocardial infarction; SD, standard deviation; NSTEMI, non-ST elevation myocardial infarction; STEMI, ST-elevation myocardial infarction; LGE-CMR, late gadolinium-enhanced cardiac magnetic resonance.

**Results**

**Clinical and Angiographic Results**

Table 1 shows the clinical characteristics of the 50 enrolled patients. Thirty-four patients presented with non-ST elevation MI and 16 with ST-elevation MI. Median peak creatine kinase MB and troponin I levels were, respectively, 15.2 ng/mL (interquartile range 8.8–51.7 ng/mL) and 3.2 ng/mL (interquartile range 1.3–8.7 ng/mL), and the mean ejection fraction was 44.7%±19.5%.

Coronary angiography was performed on median of 2 days (interquartile range 1–4 days) after the onset of ischemic symptoms. The patients received standard medical therapy, and no patient underwent coronary revascularization. Aspirin was prescribed for 45 patients (90%), clopidogrel for 30 (60%), glycoprotein 2b/3a antagonists for 4 (8%), β-blockers for 45 (90%), angiotensin-converting enzyme inhibitors for 42 (84%), statins for 36 (72%), anticoagulants for 13 (26%), nitrates for 2 (4%), diuretics for 4 (8%), and calcium antagonists for 6 (12%). No patient received thrombolytic therapy.

Echocardiography or left ventriculography did not reveal any wall motion abnormality in 10 patients. The LGE-CMR images showed that the MI was anterior in 29 patients (58%), inferior in 13 (26%), and lateral in 8 (16%). Coronary angiography showed that 25 patients had normal coronary arteries and revealed 41 nonsignificant lesions in the other 25 patients. Eighteen patients (72%) had 1-vessel disease, 5 (20%) 2-vessel disease, and 2 (8%) nonobstructive 3-vessel disease.
Coronary Computed Tomography Results

The patients underwent CTCA and CMR, respectively, a median of 6 (interquartile range 3–7 days) and 9 days (interquartile range 6–10 days) after AMI. Thirty-seven (4.9%) of the 751 coronary segments were not assessable by CT because of their small size or motion artifacts.

CTCA showed the complete absence of coronary plaques in 8 patients, and identified 101 plaques in 151 coronary vessels of the remaining 42 patients, as against the 41 plaques identified by coronary angiography. Twenty-four patients (48%) had 1-vessel atherosclerosis, 12 (24%) 2-vessel atherosclerosis, and 6 (12%) 3-vessel atherosclerosis. The median Agatston CAC score was 6 (range 0–4937); 17 patients (48%) had 1-vessel atherosclerosis, 12 (24%) 2-vessel atherosclerosis, and 6 (12%) 3-vessel atherosclerosis. The mean attenuation value in the IRAs and non-IRAs was, respectively, 79.7 ± 23 HU and 75.6 ± 29 HU (P = 0.64). Spotty calcifications were present in 17/25 mixed plaques (10/17 in IRAs and 7/8 in non-IRAs; P = 0.73).

In the 2 patients with coronary ectasia/aneurysm at coronary angiography, the CTCA findings were concordant with the invasive studies. In the patient with a suspected coronary dissection at angiography, the CTCA showed noncalcified plaque in the proximal tract of the left anterior descending artery but did not show any image suggesting coronary dissection.

Table 2. Distribution of Coronary Plaques at CTCA

<table>
<thead>
<tr>
<th>Seg. Name</th>
<th>Non-Calcified</th>
<th>Mixed</th>
<th>Calcified</th>
<th>Total</th>
<th>NA</th>
<th>Seg.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>RCA prox</td>
<td>7</td>
<td>1</td>
<td>6</td>
<td>14</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>RCA m</td>
<td>1</td>
<td>3</td>
<td>1</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>3</td>
<td>RCA d</td>
<td>0</td>
<td>1</td>
<td>3</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>4</td>
<td>PDA</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>5</td>
<td>LM</td>
<td>1</td>
<td>1</td>
<td>4</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>6</td>
<td>LAD prox</td>
<td>8</td>
<td>12</td>
<td>9</td>
<td>29</td>
<td>0</td>
</tr>
<tr>
<td>7</td>
<td>LAD m</td>
<td>7</td>
<td>4</td>
<td>9</td>
<td>20</td>
<td>1</td>
</tr>
<tr>
<td>8</td>
<td>LAD d</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>9/10</td>
<td>D1/D2</td>
<td>0</td>
<td>0</td>
<td>3</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>11</td>
<td>CFX p</td>
<td>1</td>
<td>2</td>
<td>7</td>
<td>10</td>
<td>0</td>
</tr>
<tr>
<td>12</td>
<td>CFX m</td>
<td>0</td>
<td>0</td>
<td>3</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>13</td>
<td>CFX d</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>14</td>
<td>OM1/2/RI</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>19</td>
</tr>
<tr>
<td>Total</td>
<td>27</td>
<td>25</td>
<td>49</td>
<td>101</td>
<td>37</td>
<td></td>
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Table 3. Characteristics of Infarct-Related and Non-Infarct-Related Artery Plaques

<table>
<thead>
<tr>
<th>Infarct-Related Artery Plaques (n=61)</th>
<th>Non-Infarct-Related Artery Plaques (n=40)</th>
<th>P Value</th>
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<tbody>
<tr>
<td>Non-calculated (%)</td>
<td>22 (36.1)</td>
<td>5 (12.5)</td>
</tr>
<tr>
<td>Mixed (%)</td>
<td>17 (27.8)</td>
<td>8 (20)</td>
</tr>
<tr>
<td>Calcified (%)</td>
<td>22 (36.1)</td>
<td>27 (67.5)</td>
</tr>
<tr>
<td>Plaque area (mm²)</td>
<td>6.1 ± 5.4</td>
<td>4.2 ± 2.1</td>
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<tr>
<td>Mean % stenosis</td>
<td>33.5 ± 14.6</td>
<td>31.7 ± 12.2</td>
</tr>
<tr>
<td>Remodelling index</td>
<td>1.25 ± 0.41</td>
<td>1.08 ± 0.21</td>
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Discussion

AMI patients without a significant coronary stenosis at coronary angiography represent a diagnostic challenge. The etiology of AMI in this setting is still uncertain, although the possible mechanisms include prolonged coronary artery spasm, coronary embolism, and, more probably, transient coronary thrombosis complicating a noncritical vulnerable atherosclerotic plaque. Because other clinical entities, such as myocarditis, may mimic the presentation of acute coronary syndrome, we selected only the patients whose myocardial infarction was confirmed by LGE-CMR. LGE-CMR provides detailed information concerning the characteristics of myocardial tissue and allows the detection of very small areas of fibrosis associated with myocardial infarction and other nonischemic conditions because of its high spatial resolution and contrast, and the fact that it is more sensitive than other imaging modalities such as SPECT. It is therefore the current gold standard for the in vivo identification of MI-related scarring.15–17
In patients with AMI without a critical coronary stenosis at angiography, LGE-CMR is valuable because it can confirm a diagnosis of MI and localize the infarcted area precisely to identify the probable culprit coronary artery.

In our study, CTCA revealed the presence of a significant number of atherosclerotic coronary plaques, which were underestimated by conventional coronary angiography (Figures 1 and 2). Coronary angiography is the gold standard for evaluating coronary stenosis, but it only images the lumen contour of coronary vessels and does not provide any information concerning the vessel wall and plaques. It is known that the vulnerable plaques that undergo thrombotic complications are more frequently rich in lipids, and have a large necrotic core with a thin fibrous cap, which autopsy and in vivo intracoronary ultrasonography (IVUS) studies have shown may also be present in angiographically normal

Figure 1. Example of a patient with an inferolateral myocardial infarction (late gadolinium enhancement, shown in B), coronary irregularities at coronary angiography (A), and multiple atherosclerotic plaques on the left circumflex artery detected by coronary computed tomography (2 calcified plaques arrowed in C, and a mixed plaque indicated by arrowhead in C and D). E, Short axis view of coronary plaques showing non-calcified material.

Figure 2. A patient with acute myocardial infarction, normal coronary arteries at coronary angiography (A), and late gadolinium enhancement in the antero-septal wall at cardiac MR (B). Coronary computed tomography shows a nonobstructive, eccentric mixed plaque on the proximal LAD (C) with spotty calcification (D).
Coronary arteries. Early-stage atherosclerotic plaques usually develop within the coronary wall and cause its outward remodeling with compensatory vasodilation (positive remodeling with a preserved coronary lumen) even in the presence of a significant atherosclerotic burden.

Coronary computed tomography is a reliable means of noninvasively detecting coronary atherosclerosis. Comparisons of CTCA and IVUS characterizations of plaque morphology have shown excellent agreement in identifying calcified and noncalcified plaques, and coronary remodeling. In our study, CTCA identified a significantly higher prevalence of atherosclerotic plaques in culprit coronary arteries than in nonculprit arteries. The plaques were more frequent in the proximal coronary segments, and it is known that the sites of coronary thromboses responsible for acute coronary syndromes tend to cluster within the proximal third of each vessel.

Reynolds et al used IVUS to study women without angiographically obstructive coronary artery disease who had experienced an MI, and found that plaque disruption was frequent. In agreement with our findings, they also found that the left anterior descending coronary artery was the most frequent site of plaque rupture, although they did not make a complete analysis of all coronary arteries in all of the patients.

We found a difference in the distribution of plaque types between IRAs and non-IRAs. The plaques located on culprit coronary arteries were mainly noncalcified or mixed (39/61), whereas those in nonculprit arteries were more frequently calcified (27/40). The plaques in IRAs also had a larger area. These findings are consistent with the results of previous CTCA studies comparing coronary plaque morphology in patients with acute coronary syndromes and stable coronary disease, which have shown that noncalcified lesions contribute more to total plaque burden in patients with acute coronary syndrome than in those with chronic stable coronary disease. Moreover, atherosclerotic plaques more frequently have a larger area and a positive remodeling index.

The prevalence of mixed plaques (which show a high proportion of noncalcified material in CT scans) seems to be an important aspect. Pundziute et al compared the CTCA characterization of coronary plaques with IVUS-derived virtual histological findings, and found that thinly capped fibroatheromas were more frequent in mixed than in noncalcified or calcified plaques.

We found that coronary plaques with a positive remodeling index were more frequent in IRAs, and that the mean remodeling index was higher in IRAs than non-IRAs. Conversely, there was no significant difference in stenosis between the two groups, probably because the coronary lesions were subcritical and it is known that early-stage atherosclerotic plaques tend to grow in an outward direction and cause arterial wall expansion.

The plaque attenuation values were nonsignificantly different between IRAs and non-IRAs. Motoyama et al have reported that low attenuation values (with a cut-off value of <30 HU, which may represent the lipid-rich necrotic core) identify culprit lesions in acute coronary syndrome patients with 85% accuracy. However, a recent study comparing CTCA and optical coherence tomography found limited accuracy in detecting fibrous and lipid components because of significantly overlapping CT attenuation values. Moreover, the CT attenuation measured in coronary plaques is significantly influenced by reconstruction settings and intraluminal contrast enhancement, which may vary considerably and may therefore give rise to different findings.

Spotty calcifications within plaques have also been described as potential indicators of plaque vulnerability, but we did not find any significant difference in the distribution of this calcification pattern between IRAs and non-IRAs (59% versus 87%; P = 0.73).

Seventeen of our patients had an Agatston CAC score of 0, only 8 of whom did not have any coronary plaques, thus confirming the observation that a 0 CAC score does not exclude the presence of atherosclerosis.

In our population, the CTCA demonstration of coronary plaques located in the infarct-related artery identified by means of LGE-CMR and their morphological characteristics support the pathophysiology of myocardial infarction attributable to atherosclerosis, with the disruption of mild coronary plaques, although it is not possible to exclude a different mechanism such as coronary embolism or prolonged vasospasm.

Conversely, the absence of coronary atherosclerosis at CTCA may be more indicative of an alternative etiology such as embolic myocardial infarction, and may suggest a closer follow-up to detect possibly asymptomatic arrhythmias such as atrial fibrillation.

Investigating the etiology of AMI in this setting is very important, because the prognosis is not benign and the reoccurrence of cardiovascular events is significant, with a 1-year risk of ischemic events of 4.7%. Identifying or excluding coronary atherosclerosis at an early stage may be useful to establish an appropriate therapeutic strategy for the secondary prevention of ischemic events.

**Study Limitations**

The study population was relatively small, partially because our strict inclusion criteria required an area of MI that was clearly detectable by LGE-CMR. Secondly, we did not use a comparative gold standard such as intracoronary ultrasonography or optical coherence tomography to assess plaque morphology. However, these are invasive and time-consuming techniques that cannot be used extensively in all coronary arteries, thus restricting their use to selected coronary segments and limiting their clinical applicability.

**Conclusions**

In AMI patients without critical stenoses at angiography, CTCA detects the presence of a significant number of angiographically invisible atherosclerotic plaques. The coronary plaques located on culprit vessels show a higher prevalence of noncalcified or mixed lesions whose morphological features are compatible with those of vulnerable plaques.

**Disclosures**

Dr Cademartiri is consultant for Guerbet and has received a research grant from GEHC.
References


### CLINICAL PERSPECTIVE

Almost 10% of patients with acute myocardial infarction have normal or nonsignificant coronary stenosis at coronary angiography. The absence of critical stenosis may challenge the diagnosis, however atherosclerosis may be present also in angiographically normal coronary arteries attributable to outward remodeling and acute myocardial infarction may result from disruption of nonobstructive atherosclerotic plaques. In this study, we enrolled 50 consecutive patients with acute myocardial infarction confirmed by late gadolinium–enhanced cardiac magnetic resonance without obstructive coronary stenosis at coronary angiography. In this population, coronary computed tomography angiography showed a significant number of angiographically invisible atherosclerotic plaques. Moreover, coronary plaques located on infarct-related arteries were more frequently mixed or noncalcified with higher mean plaque area and remodeling index, compatible with vulnerable plaques. These findings may support the use of optimal secondary prevention therapy to reduce the risk of recurrent events.
Computed Tomography Coronary Angiography in Patients With Acute Myocardial Infarction Without Significant Coronary Stenosis
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