Assessment of Coronary Remodeling in Stenotic and Nonstenotic Coronary Atherosclerotic Lesions by Multidetector Spiral Computed Tomography

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OBJECTIVES This study was designed to investigate whether contrast-enhanced multidetector spiral CT (MDCT) permits assessment of remodeling in coronary atherosclerotic lesions.

BACKGROUND With sufficient image quality, MDCT permits noninvasive visualization of the coronary arteries, but its ability to assess remodeling has not been evaluated.

METHODS Out of 102 patients in whom MDCT (16-slice scanner, intravenous contrast, 0.75-mm collimation, 420 ms rotation) was performed before invasive coronary angiography, 44 patients with high-quality MDCT data sets showing atherosclerotic plaque in a proximal coronary artery segment were chosen for evaluation. In multiplanar reconstructions orthogonal to the coronary artery, the cross-sectional vessel area was measured for the respective lesion and for a reference segment proximal to the lesion. The "Remodeling Index" was calculated by dividing the vessel area in the lesion by the reference segment. Results were correlated to the presence of stenosis (>50% diameter reduction) in invasive angiography. In a subset of 13 patients, MDCT measurements were verified by IVUS.

RESULTS Reference vessel area was not significantly different between nonstenotic versus stenotic lesions (20 ± 8 mm², n = 23 vs. 22 ± 8 mm², n = 21). The mean Remodeling Index was significantly higher in nonstenotic than in stenotic lesions (1.3 ± 0.2 vs. 1.0 ± 0.2, p < 0.001). In five stenotic lesions, "negative remodeling" (Remodeling Index ≤0.95) was observed. Cross-sectional vessel areas and Remodeling Indices measured by MDCT correlated closely to IVUS (r² = 0.77 and r² = 0.82, respectively).

CONCLUSIONS Multidetector spiral CT may permit assessment of remodeling of coronary atherosclerotic lesions in selected data sets of sufficient quality. (J Am Coll Cardiol 2004;43:842–7) © 2004 by the American College of Cardiology Foundation

The change of cross-sectional vessel size that occurs during the growth of atherosclerotic lesions is referred to as remodeling. Besides histopathology (1–3), intravascular ultrasound (IVUS) has been the method of choice for the investigation of coronary artery remodeling (4–14). Clinical studies using IVUS could show that variability in the process of remodeling is substantial and may be of clinical importance: Compensatory ("positive") remodeling, first described by Glagov et al. (1), delays the onset of luminal narrowing because the vessel expands with plaque enlargement, whereas inadequate compensatory remodeling is suspected to contribute to the development of focal coronary artery stenoses (6–8). Positive remodeling, on the other hand, is suspected to be associated with plaque vulnerability (9), based on both histopathologic (2,3) and clinical studies (10–14).

Under favorable conditions, multidetector spiral computed tomography (MDCT) permits noninvasive imaging of the coronary arteries with high spatial resolution (15,16) and has been shown to allow visualization of coronary atherosclerotic plaque (17–19). In order to assess whether MDCT has the potential to determine the extent of remodeling in coronary atherosclerotic lesions, we measured cross-sectional vessel areas in 43 coronary atherosclerotic lesions and their respective reference segments in selected high-quality image data sets.

METHODS

Patients scheduled for invasive coronary angiography on an inpatient basis because of suspected stable coronary artery disease were investigated by MDCT one day before the coronary angiography procedure. Exclusion criteria included an unstable clinical condition, absence of sinus rhythm, impaired renal function, and possible pregnancy. All patients gave written informed consent and the study protocol was approved by the institutional review board.

Data acquisition. All patients received 50 mg atenolol 1 h before the MDCT scan if the heart rate was >60 beats/min. MDCT data were acquired using a “Sensation 16” MDCT scanner (Siemens Medical Solutions, Forchheim, Germany). According to a previously published protocol (15,16), data were acquired with 12 × 0.75 mm collimation, a gantry rotation time of 420 ms, table feed of 2.8 mm per rotation, and tube voltage of 120 kV. The tube current was modulated...
according to the ECG with a maximum current of 500 mA during a period of 340 ms centered around 55% of the R-wave to R-wave interval and a reduction by 80% during the remaining cardiac cycle. During image acquisition, 100 ml of contrast agent were injected intravenously at a rate of 5 ml/s. Transaxial images were reconstructed in 0.5-mm intervals with a slice thickness of 1 to 0.75 mm. Image reconstruction was gated to the ECG using a half-scan reconstruction algorithm to achieve a temporal resolution of approximately 210 ms. The position of the reconstruction window within the cardiac cycle was individually optimized to minimize motion artifacts.

**Patients.** Out of 102 patients in whom MDCT and angiography were performed, 44 patients with high-quality MDCT data sets (complete absence of motion artifacts, absence of severe calcification, and high signal-to-noise ratio upon visual inspection) as well as identifiable atherosclerotic plaque in the left main coronary artery (LM) (n = 7) or proximal section of the left anterior descending (LAD) (n = 20), left circumflex coronary artery (LCX) (n = 1), or right coronary artery (RCA) (n = 16) were selected for further evaluation. Clinical characteristics of the patients are given in Table 1. The mean heart rate during the scan was 59 ± 10 beats/min (43 to 97 beats/min).

**MDCT data analysis.** MDCT data were transferred to an offline image analysis workstation (Leonardo, Siemens Medical Solutions, Forchheim, Germany). After identifying the atherosclerotic lesions in the original MDCT data sets, serial multiplanar reconstructions (slice thickness 1 mm) were rendered in an orientation perpendicular to the longitudinal axis of the respective coronary artery segment (Figs. 1 and 2). Using a fixed image display setting (window 700 Hounsfield units [HU], level 250 HU), the image that displayed maximum luminal narrowing was identified by visual estimation and the outer vessel contour (border to low-signal epicardial fat) was manually traced to measure the cross-sectional vessel area. Similarly, the cross-sectional vessel area was determined in a reference segment without detectable plaque proximal to and as close as possible to the respective coronary lesion (in absence of a segment without plaque, the least diseased segment between the lesion and the coronary ostium or major bifurcations).

**Invasive coronary angiography and intravascular ultrasound.** Invasive coronary angiograms were evaluated by quantitative coronary angiography (QuantCor.QCA, Pie Medical Systems, Maastricht, Netherlands). A significant coronary artery stenosis was defined as a mean diameter reduction in two projections ≥50%. In 13 patients, IVUS of the respective artery was performed as part of the invasive diagnostic procedure (motorized pullback at 0.5 mm/s, 40 MHz, Atlantis, Boston Scientific, Natick, Massachusetts). The lesions visualized by MDCT were identified in IVUS using fiducial landmarks such as bifurcations and branches as well as plaque morphology, and the cross-sectional vessel area was measured by an independent observer by tracing the external elastic membrane at the site of maximum luminal narrowing and in the proximal reference segment (segment without plaque proximal to the respective lesion or, should no segment without plaque be available, the least diseased segment between the lesion and the coronary ostium or major bifurcations).

**Statistics.** The Remodeling Index was calculated by dividing the cross-sectional vessel area at the site of maximum luminal narrowing by the cross-sectional vessel area in the reference segment. MDCT-derived vessel areas and remodeling indices in stenotic and nonstenotic lesions were compared using a Mann-Whitney U Wilcoxon rank-sum test. Vessel areas and remodeling indices determined in IVUS and MDCT were compared using Pearson’s correlation and Bland-Altman analysis.

**RESULTS**

Quantitative coronary angiography revealed a significant coronary stenosis in 21 patients (LM: 5, LAD: 9, RCA: 7, mean diameter reduction: 76 ± 10%, range: 63 to 94%). In 23 patients, no significant stenosis was present (LM: 2, LAD: 11, LCX: 1, RCA: 9, mean diameter reduction: 22 ± 12%, range: 0 to 41%). In MDCT, there was no significant difference in the mean reference cross-sectional vessel area in the 23 nonstenotic lesions (19 ± 8 mm²) as compared to the 21 stenotic lesions (22 ± 8 mm², p = 0.1). The mean cross-sectional vessel area at the site of maximum luminal obstruction was 26 ± 11 mm² in nonstenotic lesions as

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**Table 1.** Patient Characteristics in the Total Study Group as well as in the 23 Patients Without and 21 Patients With a Coronary Stenosis Exceeding 50% Diameter Reduction

<table>
<thead>
<tr>
<th></th>
<th>All</th>
<th>Nonstenotic Lesions</th>
<th>Stenotic Lesions</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>44</td>
<td>23</td>
<td>21</td>
<td></td>
</tr>
<tr>
<td>Men/women</td>
<td>33/11</td>
<td>20/3</td>
<td>13/8</td>
<td>n.s.</td>
</tr>
<tr>
<td>Age (yrs)</td>
<td>62 ± 12</td>
<td>60 ± 11</td>
<td>63 ± 12</td>
<td>n.s.</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>80 ± 10</td>
<td>81 ± 9</td>
<td>79 ± 11</td>
<td>n.s.</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>29 (67%)</td>
<td>15 (65%)</td>
<td>14 (64%)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Smoking</td>
<td>20 (47%)</td>
<td>11 (48%)</td>
<td>9 (43%)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Hypertension</td>
<td>33 (77%)</td>
<td>16 (70%)</td>
<td>17 (81%)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Diabetes</td>
<td>8 (18%)</td>
<td>5 (22%)</td>
<td>3 (14%)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Family history</td>
<td>18 (42%)</td>
<td>10 (43%)</td>
<td>8 (38%)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Remodeling Index</td>
<td>1.2 ± 0.2</td>
<td>1.3 ± 0.2</td>
<td>1.0 ± 0.2</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

MDCT = multidetector spiral computed tomography; n.s. = not significant
compared to 22 ± 10 mm² in stenotic lesions (p = 0.2). As determined by MDCT, the mean Remodeling Index of nonstenotic lesions was 1.3 ± 0.2 whereas it was 1.0 ± 0.2 for stenotic lesions (p < 0.001, Fig. 3). In five stenotic coronary artery lesions, but no nonstenotic lesions, a Remodeling Index ≤0.95 (“negative remodeling” or “constrictive remodeling” [6–10]) was observed. The mean Remodeling Index in 24 lesions that contained calcium (1.2 ± 0.2) and 20 lesions that did not contain calcium in MDCT (1.1 ± 0.3) was not significantly different.

The MDCT-derived cross-sectional vessel areas were compared to IVUS in 13 patients (26 sites, mean MDCT: 20 ± 7 mm², mean IVUS: 18 ± 8 mm²). The mean absolute difference was 3 ± 3 mm² (range 0 to 8 mm²), or

Figure 1. Visualization of coronary plaque and assessment of remodeling by multidetector spiral computed tomography (MDCT). (A–D) Patient with a not significantly stenotic lesion in the proximal left anterior descending coronary artery. (A) X-ray coronary angiogram (arrow = site of the lesion); (B) axial MDCT image (1-mm slice thickness) at the level of the lesion (arrow); (C) MDCT reconstruction orthogonal to the vessel at the site of maximum luminal obstruction showing circumferential plaque (cross-sectional vessel area 41 mm²); (D) MDCT reconstruction orthogonal to the vessel in the reference segment (cross-sectional vessel area 35 mm²). Remodeling Index 1.2. (E–H) Patient with a high-grade stenosis of the left anterior descending coronary artery. (E) X-ray coronary angiogram (arrow = left anterior descending coronary artery stenosis); (F) axial MDCT image (1.0 mm slice thickness) at the level of the partly calcified lesion (arrow); (G) MDCT reconstruction orthogonal to the vessel at the site of maximum luminal obstruction (cross-sectional vessel area 22 mm²); (H) MDCT reconstruction orthogonal to the vessel in the reference segment (cross-sectional vessel area 22 mm²). Remodeling Index 1.
16% of the mean value of IVUS and MDCT. Bland-Altman analysis showed a bias towards larger vessel areas in MDCT (mean difference: 1.2 mm², Fig. 4). Similarly, Pearson’s correlation was \( r^2 = 0.77 \) (\( p < 0.001 \)) with a slope of the regression line of 0.82 and a positive intercept caused by overestimation, especially of small cross-sectional vessel areas by MDCT. In the 13 patients investigated by MDCT and IVUS, the mean Remodeling Index was 1.1 ± 0.3 in MDCT and 1.1 ± 0.4 IVUS (\( r^2 = 0.82, p = 0.001 \), Fig. 4).

DISCUSSION

The use of contrast-enhanced MDCT for the detection of coronary artery stenoses and for the detection and analysis of coronary atherosclerotic plaque has been described (15–19). The assessment of remodeling in coronary atherosclerotic lesions may add additional information about the propensity of a plaque to rupture and cause coronary events (2,3,9–14). Thus, if MDCT imaging for risk assessment were considered, the ability of MDCT to determine the extent of remodeling in coronary atherosclerotic lesions could be useful. The recent introduction of MDCT scanners with sub-millimeter slice collimation increased the spatial resolution as compared to previous scanner generations and made the reconstruction of near-isotropic data sets possible. These scanners should thus improve the ability to measure vessel dimensions. So far, the ability and accuracy of MDCT to determine the extent of
coronary remodeling have not been evaluated. As a first step towards verifying the ability of MDCT to noninvasively assess coronary remodeling, we analyzed selected MDCT data sets with high image quality and determined the extent of remodeling in 43 coronary atherosclerotic lesions that were detectable by MDCT. In a subset of 13 patients, IVUS was performed to verify the accuracy of MDCT measurements, and cross-sectional vessel areas measured in MDCT correlated closely to the external elastic membrane area measured in IVUS. The relationship between the extent of remodeling in MDCT and the degree of stenosis in invasive angiography served as an additional—albeit weak—verification, because it is known that the Remodeling Index differs between stenotic and nonstenotic lesions. As expected (6–8), we could demonstrate a lesser degree of remodeling in lesions with a significant (>50%) lumen reduction as compared to nonstenotic coronary artery lesions.

**Study limitations.** Our study is clearly limited by the fact that coronary vessel dimensions and the degree of remodeling could not be validated in all 44 patients against IVUS. Also, this study served as a proof of principle by limiting analysis to extremely selected patients chosen for high MDCT image quality and absence of artifacts, for example, caused by remaining motion and severe calcification (15,16). Because the vessel size is often smaller and image quality is reduced, only one lesion in the left circumflex coronary artery was analyzed. Furthermore, a relatively simple definition of the reference segment was used in MDCT and IVUS. Also, it has not yet been clarified which structures of the arterial wall actually contribute to the measurement of cross-sectional vessel areas in MDCT. One fixed window and level setting was used for vessel dimension measurements in MDCT images and, so far, no histopathologic

**Figure 3.** Remodeling Indices as determined by multidetector spiral computed tomography in 23 nonstenotic (mean: 1.3 ± 0.2) and 21 stenotic lesions (mean: 1.0 ± 0.2, p < 0.001). Large bars = mean value; thin bars = mean value ± SD.

**Figure 4.** (A) Correlation of cross-sectional vessel areas in intravascular ultrasound (IVUS) and multidetector spiral computed tomography (MDCT) (n = 26, r² = 0.77); (B) Bland-Altman analysis of the differences in cross-sectional vessel areas measured in MDCT and IVUS (mean difference: 1.2 ± 3.7 mm²). The dashed lines correspond to the mean difference ± 2 SD (−6.10 to +8.5 mm²); (C) correlation of Remodeling Indices (RI) in IVUS and MDCT (n = 13, r² = 0.82).
investigations have been performed as to the CT density of various layers of the arterial wall. However, the thickness of nondiseased coronary arterial wall is well below the spatial resolution of MDCT, which is limited by the slice thickness (0.75 to 1 mm). The arterial wall itself thus only becomes detectable in MDCT when thickened through atherosclerosis, and the atherosclerotic plaque itself will then contribute most to the dimensions of the depicted wall. Similarly, except for the lumen itself, the atherosclerotic plaque is what contributes most to the external elastic membrane area measured in IVUS (9). Finally, the presence of calcium may have confounded measurements of vessel cross-sections because of partial volume effects. However, segments with severe calcification were not included in the analysis and no statistically significant difference between the Remodeling Indices derived in MDCT cross-sections with and without detectable calcium was observed. A separate, nonenhanced coronary calcium scan was not performed in order to reduce the overall radiation exposure.

In spite of the limitations, the results illustrate the method’s potential for depicting coronary artery anatomy and pathology. Correlations of vessel dimensions and Remodeling Indices to IVUS were close. Overestimation by MDCT, especially of smaller vessel dimensions, can be explained by partial volume effects, which are caused by the substantially lower spatial resolution of the reformatted MDCT images as compared to IVUS. As expected, a significantly lesser degree of remodeling was found in lesions that were associated with significant luminal obstruction. Other investigators have suggested the use of magnetic resonance imaging for the in vivo assessment of coronary artery remodeling (21,22), but the available data, both on magnetic resonance and MDCT, currently are far too limited to speculate on the clinical applicability of either method. However, their noninvasive nature makes both methods attractive candidates for further development, especially when the cost and risk of IVUS, the current standard, are considered. Should further technical improvements permit reliable noninvasive assessment of coronary arterial remodeling in the majority of patients, such information may be useful for prognostic purposes because positive remodeling has been shown to be intricately associated with plaque vulnerability (2,3,11–14). The degree of remodeling could thus add to the information that magnetic resonance imaging and MDCT can noninvasively provide about coronary atherosclerotic lesions in an individual (23) in an attempt to optimize further diagnostic and therapeutic measures.

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REFERENCES


