Noninvasive Evaluation of the Coronary Arteries With Multislice Computed Tomography in Hypertensive Patients

Joanne D. Schuijf, Jeroen J. Bax, J. Wouter Jukema, Hildo J. Lamb, Hubert W. Vliegen, Ernst E. van der Wall, Albert de Roos

Abstract—Because patients with hypertension are at increased risk for coronary artery disease, early and noninvasive identification of the disease in patients with hypertension is important. Recently, multislice computed tomography (MSCT) has been demonstrated to allow both noninvasive coronary angiography and assessment of left ventricular function. The purpose of the present study therefore was to demonstrate the feasibility of this approach in patients with hypertension with known or suspected coronary artery disease and to compare the results to invasive coronary angiography and 2-dimensional echocardiography, respectively. MSCT was performed in 31 patients with confirmed hypertension. From the MSCT images, the presence of significant coronary stenoses (≥50% luminal narrowing) and regional wall motion abnormalities were evaluated and compared with invasive coronary angiography and 2-dimensional echocardiography. In addition, left ventricular ejection fraction was calculated from the MSCT images. A total of 243 (88%) coronary artery segments could be evaluated with MSCT. Sensitivity and specificity for the detection of significant coronary artery stenoses were 93% and 96%. On a per-patient basis, MSCT was accurate in 28 (90%) patients. Mean left ventricular ejection fraction was 46±14% (range, 16% to 64%). The agreement for assessing regional wall motion was 91% (kappa statistic, 0.81). In conclusion, simultaneous, noninvasive evaluation of coronary artery stenoses and left ventricular function with MSCT is accurate in patients with hypertension. This noninvasive approach may allow triage of patient treatment in terms of conservative versus invasive management. (Hypertension. 2005;45:227-232.)

Key Words: coronary artery disease • imaging

Coronary artery disease (CAD) is the major cause of morbidity and mortality in hypertensive patients, especially because patients with hypertension are at increased risk for CAD as compared with normotensive individuals. Moreover, because hypertension is present in 1 of every 5 adults, noninvasive detection of CAD in this particular patient group has become a clinically important issue. However, of several noninvasive tests, including exercise electrocardiography and myocardial perfusion imaging, a limited specificity in hypertensive patients has been reported because of an increased occurrence of false-positive results in this particular patient group. These positive test results may represent impaired vasodilator reserve and increased myocardial oxygen demand as a consequence of microvascular disease, and thus myocardial ischemia in the absence of significant coronary artery abnormalities. A noninvasive test therefore should ideally allow direct visualization of the coronary arteries to detect or exclude obstructive CAD to triage patients for optimal medical therapy or invasive evaluation.

Over recent years, multislice computed tomography (MSCT) has emerged as a potential noninvasive imaging method that allows the acquisition of high-quality images of the entire heart within a single breath-hold. High sensitivities and specificities in the detection of coronary artery stenoses have been reported, ranging from 72% to 95% and 75% to 99%, respectively. Furthermore, the simultaneous recording of the electrocardiogram permits the reconstruction of images at any moment of the cardiac cycle, thus allowing cardiac function analysis in addition to the evaluation of the coronary arteries, although data are scarce.

Because no specific data are available on the performance of MSCT in patients with hypertension, the purpose of the present study was to demonstrate the feasibility of evaluation of the coronary arteries and left ventricular (LV) function using MSCT in patients with hypertension. Conventional coronary angiography and 2-dimensional echocardiography served as reference standards.

Methods

Patients and Study Protocol

The study group comprised 31 patients with chest pain and/or dyspnea and confirmed hypertension (defined by sequential separate...
occasions of blood pressure measurements using an arm cuff and a mercury manometer). All patients were scheduled for conventional coronary angiography for the evaluation of chest pain/dyspnea symptoms. Hypertension was defined as systolic blood pressure $\geq 140$ mm Hg and/or diastolic blood pressure $\geq 90$ mm Hg, and/or use of antihypertensive medication.

Patients with atrial fibrillation were excluded, and additional exclusion criteria were renal insufficiency (serum creatinine $\geq 120$ mmol/L), known allergy to iodine contrast media, severe claustrophobia, and pregnancy.

All patients gave informed consent to the study protocol, which was approved by the local ethics committee.

**Data Acquisition**

In the initial 17 patients, MSCT angiography was performed with a Toshiba Multi-Slice Aquilion 0.5 system and in the remaining patients with a Toshiba Multi-slice Aquilion 16 system (Toshiba Medical Systems, Otawara, Japan). Thus, detector collimation was either $4\times2.0$ mm or $16\times0.5$ mm. Other parameters were rotation time 400, 500, or 600 ms (depending on the heart rate), tube current 250 mA, and tube voltage 120 kV. A bolus nonionic contrast (Xenetix 300; Guerbet, Aulnay S. Bois, France) was injected in the antecubital vein at a flow rate of 4.0 mL/s, resulting in a total administered dose of 120 to 150 mL, depending on the scan time. Automated detection of peak enhancement in the aortic root was used for timing of the scan. During a breath-hold of $\approx 25$ seconds, cardiac images, from the aortic root to the apex, were acquired. Data were reconstructed using retrospective electrocardiographic gating. A multisegment reconstruction algorithm was applied, meaning that data from up to 4 consecutive heartbeats were used to generate a single image, thereby resulting in a temporal resolution of 105 to 200 ms. Spatial resolution was $0.5\times0.5\times2.0$ mm and $0.5\times0.5\times0.5$ mm for the 4-slice and 16-slice system, respectively. No $\beta$-blocking medication to reduce the heart rate was administered before the examination and patients were included regardless of heart rate.

To evaluate the presence of coronary artery stenoses, reconstructions in diastole (65% to 85% of the cardiac cycle) were generated with a reconstructed section thickness of either 1.0 mm (4-slice system) or 0.4 mm (16-slice system). Images were transferred to a remote workstation (Vitrea2; Vital Images, Plymouth, Minn) for postprocessing and evaluation. Images containing the fewest motion artifacts were used for evaluation.

For the evaluation of LV function, the same original raw data set (acquired for the evaluation of the coronary arteries) was used. Images were reconstructed retrospectively at 20 time points, starting at early systole (0% of the cardiac cycle) to the end of diastole (95% of the cardiac cycle). Subsequently, short-axis images with a slice thickness of 2.00 mm were generated and transferred to a remote workstation with dedicated cardiac function analysis software (MR Analytical Software System [MASS], Medis, Leiden, the Netherlands).

**Data Analysis**

The images were evaluated by an experienced observer blinded to the catheterization results. A modified AHA–ACC segmentation model was used for stenosis assessment: the left main coronary artery (segment 5), the right coronary artery (segments 1, 2, and 3), the left anterior descending coronary artery (segments 6, 7, and 8), and the left circumflex artery (segment 11 and 13). All present and of sufficient size (diameter $>2.0$ mm), distal segments and side branches (segments 4, 9, 10, 12, 14, 15, 16, and 17) were also evaluated.

In addition to the original axial slices, curved multplanar reconstructions and 3-dimensional volume-rendered reconstructions were used to assess the presence of luminal narrowing. First, assessability was determined for each segment. Interpretable segments were subsequently classified as having significant stenosis ($\geq 50\%$ reduction of lumen diameter) or not.

<table>
<thead>
<tr>
<th>TABLE 1. Clinical Characteristics of the Study Population (n=31)</th>
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<tbody>
<tr>
<td>Characteristic</td>
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<tr>
<td>Gender, M/F</td>
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<tr>
<td>Age, y</td>
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<tr>
<td>Hypertension</td>
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<tr>
<td>Heart rate during data acquisition, bpm</td>
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<td>$\beta$-blocker medication</td>
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<td>Angina pectoris</td>
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<td>CCS class 1/2</td>
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<tr>
<td>CCS class 3/4</td>
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<tr>
<td>Heart failure</td>
</tr>
<tr>
<td>NYHA class 1/2</td>
</tr>
<tr>
<td>NYHA class 3/4</td>
</tr>
<tr>
<td>History</td>
</tr>
<tr>
<td>Previous MI</td>
</tr>
<tr>
<td>Previous PCI/CABG</td>
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<tr>
<td>Other risk factors for CAD</td>
</tr>
<tr>
<td>Diabetes type 2</td>
</tr>
<tr>
<td>Smoking</td>
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<tr>
<td>Hypercholesterolemia</td>
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<tr>
<td>Family with CAD</td>
</tr>
</tbody>
</table>

Data between parentheses are %.

bpm indicates beats per minute; CABG, coronary artery bypass grafting; CAD, coronary artery disease; CCS, Canadian Cardiovascular Society; MI, myocardial infarction; NYHA, New York Heart Association; PCI, percutaneous coronary intervention.

**Figure 1.** Severe lesion in the left anterior descending coronary artery (LAD). A, A curved multiplanar MSCT reconstruction of the LAD is shown, demonstrating a severe stenosis (white arrowhead) in the proximal part of the vessel. A 3-dimensional volume-rendered reconstruction is provided in (B). The severe lesion is also clearly visible in (C) (black arrowhead), an enlargement of (B). Findings were confirmed by conventional angiography (D).
An experienced observer blinded to all other data evaluated the presence of regional wall motion abnormalities visually on the short-axis slices (displayed in cine-loop format) using a previously described 17-segment model. Each segment was graded on a 4-point scale (1 = normokinesia, 2 = hypokinesia, 3 = akinesia, and 4 = dyskinesia).

To calculate LV ejection fractions, endocardial contours were manually drawn on both the end-systolic and end-diastolic short-axis images. Papillary muscles were regarded as being part of the LV cavity. LV end-systolic and end-diastolic volumes were calculated using commercially available software (MASS) developed at our institution by summation of the product (area × slice distance) of all slices. Finally, the related LV ejection fraction was derived by subtracting the end-systolic volume from the volume at end-diastole and dividing the result by the end-diastolic volume.

### Invasive Coronary Angiography

Invasive coronary angiography was performed according to standard techniques. Vascular access was obtained through the femoral approach with Seldinger technique and a 6-French or 7-French catheter. Coronary angiograms were visually evaluated by an experienced observer without knowledge of the MSCT data. The same segmentation as described for MSCT was applied to determine the presence of significant luminal reduction in each coronary segment.

### 2-Dimensional Echocardiography

Two-dimensional echocardiography was performed in the left lateral decubitus position using a commercially available system (Vingmed System FiVe/Vivid-7; GE-Vingmed, Milwaukee, Wis). Images were acquired using 3.5-MHz transducer at a depth of 16 cm in standard parasternal and apical views.

Regional wall motion was scored using the 17-segment model and 4-point scale as described for MSCT.

### Statistical Analysis

Sensitivity, specificity, and positive and negative predictive values were calculated using the following formula:

\[ P = \frac{1.96 \times \sqrt{\left( \frac{p \times (100-p)}{n} \right)}}{\sqrt{n}} \]

where \( p \) = sensitivity or specificity (%) and \( n \) = the total number of segments. Additionally, data were analyzed on a per-patient basis. MSCT was considered correct in the individual patient analysis if at least 1 significant stenosis was detected on the MSCT images or if MSCT ruled out the presence of any significant stenosis. Agreement for regional wall motion was expressed in a 4 × 4 table using weighted \( \kappa \) statistics. A \( \kappa \) value of <0.4 represents poor agreement, a \( \kappa \) value between 0.4 and 0.75 represents fair to good agreement, and a \( \kappa \) value of >0.75 is considered an excellent agreement based on the Fleiss classification. \( P < 0.05 \) was considered to indicate statistical significance.

### Results

#### Patient Characteristics

The patient characteristics are listed in Table 1. The study group consisted of 31 patients with confirmed hypertension; mean systolic blood pressure was 138 ± 21 mm Hg (range, 110 to 167 mm Hg), whereas mean diastolic blood pressure was 81 ± 10 mm Hg (range, 67 to 105 mm Hg). Average duration of hypertension at the time of MSCT was 3.1 ± 5.8 years (range, 0 to 9 years). Mean LV mass, as determined by echocardiography, was 197 ± 68 grams. Mean body mass index was 25 ± 3 kg/m². Cardiac medication was continued during the study period. A total of 23 patients (74%) used \( \beta \)-blockers. Other medications included angiotensin-converting enzyme inhibitors (n = 25), calcium antagonists (n = 16), nitrates (n = 13), diuretics (n = 10), oral anticoagulants (n = 30), and statins (n = 30).

The average interval between conventional coronary angiography and MSCT was 1.9 ± 2.7 days. The interval between 2-dimensional echocardiography and MSCT was 2.2 ± 1.8 days.

#### Coronary Artery Stenoses

A total of 277 coronary segments were available for comparison between conventional angiography and MSCT. Of these...
segments, 243 (88%) were of sufficient quality to evaluate the presence of significant (≥50%) narrowing. Reasons of uninterpretability were predominantly the presence of coronary stents and motion artifacts. Furthermore, the majority of uninterpretable segments were located in distal segments (segments 3, 8, and 13). Conventional angiography revealed 57 significant stenoses in the interpretable segments. Of these lesions, 53 were correctly detected by MSCT. The presence of significant stenosis was correctly ruled out in 179 out of 186 nondiseased segments. Accordingly, the sensitivity and specificity for the detection of coronary artery stenoses were 93% and 96%, respectively. Details per coronary artery, including positive and negative predictive values, are summarized in Table 2; among the different coronary arteries, no significant differences were noted. On a per-patient basis, MSCT was accurate in 28 (90%) patients. Of 21 patients with significant lesions on conventional angiography, 20 (95%) patients were correctly identified. In the remaining 10 patients with no significant abnormalities, MSCT was accurate in 8 (80%) patients. In Figures 1 and 2, MSCT images of both stenotic and normal coronary arteries are shown. Of note, to obtain a multiplanar reconstruction, each vessel needs to be reconstructed separately. Thus, no side branches are visible, because only multiplanar reconstructions of the 3 major vessels are provided.

LV Function
LV ejection fraction, as determined by MSCT, ranged from 16% to 64% (mean 46±14%), respectively. Abnormal wall motion was observed in 158 (30%) of 527 segments, with 86 (54%) of these segments showing hypokinesia, 55 (35%) akinesia, and 17 (11%) dyskinesia. In 148 (94%) of these segments, MSCT also demonstrated abnormal wall motion. Overall, 91% of segments were scored identically on both modalities (kappa statistic, 0.81; Table 3), indicating an excellent agreement between 2-dimensional echocardiography and MSCT. For the individual wall motion scores (1–4), agreements were 97%, 78%, 71%, and 94%, respectively. Examples of short-axis reconstructions are shown in Figures 3 and 4, showing patients with normal and abnormal LV function.

Discussion
The results of the current study demonstrate that accurate evaluation of the coronary arteries and LV function in patients with hypertension using contrast-enhanced MSCT is feasible. In the detection of significant coronary artery stenoses, an excellent sensitivity and specificity of 93% and 96% were demonstrated. These results are in line with previous studies obtained in the general patient population. In a study by Ropers et al., 19 coronary artery stenoses were detected with a sensitivity and specificity of 91% and 93%, respectively. A somewhat higher sensitivity (95%) and slightly lower specificity (89%) were reported by Nieman et al. 16 In both studies, a negative predictive value of 97% was reported, similar to our results (98%). These findings demonstrate the potential of MSCT to function as a diagnostic tool to rule out the presence of CAD. This may improve the noninvasive workup of patients with hypertension in particular, because in these patients false-positive test results in the absence of coronary artery stenoses are frequently encountered with other noninvasive imaging modalities, including nuclear perfusion imaging and stress echocardiography. 3 These imaging modalities visualize the consequences of ischemia (induction of perfusion abnormalities or systolic wall motion abnormalities). In contrast, direct visualization of the coronary arteries is allowed by MSCT. Thus, by ruling out the presence of CAD, noninvasive angiography with MSCT may substantially reduce the number of patients who will need diagnostic invasive coronary angiography. However, when significant abnormalities are observed on the MSCT images, this information could be used for a more efficiently targeted (interventional) treatment strategy. Still, further prognostic studies are needed in larger cohorts before MSCT can become an established diagnostic modality and replace conventional coronary angiography in certain patient groups.

In addition to noninvasive coronary angiography, LV function analysis was performed. Agreement of regional wall

<table>
<thead>
<tr>
<th>Echocardiography</th>
<th>MSCT</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
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<tr>
<td>2</td>
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<tr>
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<td>9</td>
<td>39</td>
<td>1</td>
<td>1</td>
<td>9</td>
<td>49</td>
</tr>
<tr>
<td>4</td>
<td>0</td>
<td>3</td>
<td>16</td>
<td>19</td>
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<td>19</td>
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<tr>
<td><strong>Total</strong></td>
<td>369</td>
<td>86</td>
<td>55</td>
<td>17</td>
<td>527</td>
<td></td>
</tr>
</tbody>
</table>

1 indicates normokinesia; 2, hypokinesia; 3, akinesia; 4, dyskinesia.
motion scores was excellent, with 91% of segments scored identically, resulting in a kappa statistic of 0.81. For the individual wall motion scores, agreement was highest for segments with either normal contractility (97%) or dyskinesia (94%), whereas it was slightly lower in segments with intermediate motion abnormalities (75%). This phenomenon may be attributed to the temporal resolution of the technique (105 to 200 ms), which may be insufficient to allow detection of subtler wall motion abnormalities in some cases. For echo, wall motion was derived from parasternal and apical views, whereas only short-axis views were used with MSCT, and this may also account for discrepancies.

In contrast to several other studies, no β-blocking agents were administered before the MSCT data acquisition to lower heart rates >65 beats per minute. The use of a multisegmented reconstruction algorithm, available on our MSCT equipment, allowed the inclusion of patients with higher heart rates without compromise to temporal resolution.

Limitations of the Present Study
First, a 4-slice system and 16-slice system were used for data acquisition. Because 16-slice systems have been demonstrated to result in better assessability and accuracy as compared with 4-slice systems, the use of 2 different systems is likely to have influenced our results. Moreover, of the 34 coronary artery segments with insufficient quality to assess the presence or absence of significant coronary artery stenoses, 68% were acquired with the 4-slice system. As expected, assessability was lowest in the right coronary artery, because this vessel displays the fastest movement during the cardiac cycle. In addition, the presence of coronary stents also frequently resulted in degraded image quality. Similar percentages have been reported previously. In the near future, however, this limitation may be overcome by the introduction of 32-detector and 64-detector row scanners in combination with faster rotation times, which are likely to reduce the percentage of nonassessable segments. Second, an important drawback of MSCT is the radiation dose that is still considerably high: ≈8 mSv. However, with the use of new filters, the radiation dose will decrease substantially. Third, precise quantification of luminal stenosis (as can be performed with angiography) is currently not possible with MSCT, because the spatial resolution is still suboptimal and validated software is currently not available. Finally, the prevalence of CAD in the present population was high and validation of the technique in patients with lower prevalence of CAD is warranted. Similarly, patients with late-stage as well as early-stage hypertension were included, because the purpose of the present study was to demonstrate the feasibility of the technique in this population. Thus, further testing of the technique in patients with early-stage hypertension is needed. In conclusion, accurate simultaneous evaluation of the coronary arteries and LV function in patients with hypertension is feasible.

Perspectives
This combined strategy may offer a new approach for a noninvasive, conclusive workup in patients with hypertension and known or suspected CAD. Direct visualization of the coronary arteries may result in improved identification of patients at risk for cardiovascular events. However, whether this translates into improved clinical management still needs to be tested, particularly in patient groups with early-stage hypertension and lower prevalence of CAD.

Acknowledgments
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References


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