Case report

Noninvasive evaluation of coronary artery plaque with electrocardiographically-gated multislice computed tomography

Shinro Matsuo*, Ichiro Nakae, Tetsuya Matsumoto, Minoru Horie

Department of Cardiovascular and Respiratory Medicine, Shiga University of Medical Science, Seta, Otsu, Shiga 520-2192, Japan

Received 30 August 2004; revised 29 March 2005; accepted 29 March 2005

Abstract

The study evaluated the feasibility of determining coronary lesion configuration, including coronary plaque, stenosis and calcification, by ECG-gated MSCT. The results were compared with the characteristics of intravascular ultrasound (IVUS). The overall sensitivity for diagnosing significant coronary stenosis was 80.2%, and the specificity was 95.6%. There were significant differences in plaque density among three groups \((p<0.01)\). MSCT was feasible for the detection of coronary artery stenosis. And plaque composition could be clearly differentiated and classified by MSCT, which is a promising method of non-invasive risk assessment in patients with known or suspected coronary artery disease.

© 2005 Elsevier Ltd. All rights reserved.

Keywords: Multislice CT; Coronary artery imaging

1. Introduction

Coronary plaque rupture and subsequent thrombosis are major components of unstable plaque, which characterize the transition from stable coronary artery disease to acute coronary syndrome. Intravascular ultrasound (IVUS), unlike coronary angiography, allows for visualization of changes in the vessel wall, the site of development of atherosclerotic plaques. At present, IVUS is the most reliable method of detecting early plaque size. However, IVUS requires invasive procedures in the catheter laboratory [1] and has limitations for widespread clinical use. A non-invasive approach would be more preferable.

The introduction of multi-slice computed tomography (MSCT) has greatly benefited cardiovascular CT imaging applications. The high speed of image acquisition shortens breath-hold and examination times for the patient and reduces the amount of contrast media needed for high and consistent vascular enhancement.

The study assessed the feasibility in determining coronary lesion configuration, including coronary plaque, calcification and stenosis, by ECG-gated MSCT.

2. Methods

2.1. The study population

The study group consisted of patients with suspicion of coronary artery disease referred to our university hospital. Fifty patients underwent both elective coronary angiography and MSCT. Thirty-five men and 15 women, aged 43–79 years (mean age 62 years), were included in the study. All patients showed normal sinus rhythm on CT examination day. The conventional coronary angiogram was obtained within 2 weeks of the data of the CT examination. Informed consent was obtained from all patients.

2.2. Multislice computed tomography: data acquisition and image reconstruction

The MSCT scanner (the Aquilion, Toshiba, Tokyo, Japan) with a 500-ms rotation time and simultaneous acquisition of eight slices were used. Patients were given
oral metoprolol (40 mg p.o.) 1–2 h prior to the MSCT scan to lower a heart rate. Twenty patients received beta-blocker, three of these 20 patients could not achieve a heart rate less than 70/min. First, a fast localization scan was performed to determine the boundaries of the heart. The range of the heart (120 mm) was covered in one breath hold period of 25 s. Table feed was 3.0-mm/s (helical pitch 2.0). The normal scanning parameters were set to 120 kV, 300 mA, 500-ms rotation time using an 8×1-mm collimation. These parameters were applied throughout the entire scan without dose modulation in the study [2]. The scanning delay was determined by injecting 15 mL of contrast agent (Optiray 320, Tyco Healthcare Japan, Inc.) with a 3-mL/sec flow rate and scanning every 2 s in the ascending aorta at the main pulmonary artery. After imaging at the level of the carina and positioning the region of interest (ROI) in the center of the ascending aorta, contrast agent was injected and the scanning delay was then determined as the interval from the start of the injection to peak enhancement in the ascending aorta. An additional 3-s delay was chosen to ensure passage of the contrast material into the coronary vessels before the onset of scanning, especially in patients with low cardiac output. Coronary vessel enhancement was achieved with i.v. injection of 85 mL of contrast agent with a 3-mL/sec flow rate, and the scan was initiated with a delay according to the previously determined contrast agent transit time. Contrast-enhancement was used to enable identification of all major epicardial vessels, which is essential for future dosimetric studies. The images were reconstructed by ECG-gated segment reconstruction. The images were obtained during the time of least motion or between the T and P waves, to avoid cardiac motion artifacts occurring during the ventricular rapid filling and atrial contraction periods. The reconstruction window was positioned so that the end of the reconstruction period was positioned at the peak of the P wave on ECG. Since the right coronary artery and left circumflex are closer to atria than the left anterior descending coronary artery, and are affected by atrial contraction, we added reconstruction of multiple sets of images in different set of cardiac cycle to optimize vascular visualization.

2.3. Interpretation of MSCT data

Two observers with no knowledge of the results of the coronary angiograms independently assessed the original and reformatted MSCT images. The coronary tree was divided into proximal, middle, and distal segments according to AHA guidelines [3]. The maximum intensity projections with a slice thickness of 2–6 mm, depending on the presence of adjacent structures or coronary calcifications, were used to screen for coronary stenosis. Multiplanar reconstructions were used to obtain more detailed information. In the analyses, the vessel diameters of the target vessels were measured at the defined sites using axial slices by focusing on vessel-connecting tissue interface. At each site, the vessel-connecting tissue interface was identified as having a lower density than contrast media-filled coronary artery (Fig. 1). The four major epicardial coronary arteries and the right coronary artery were assessed as having hemodynamically significant coronary artery stenosis (>50% in diameter) or not [4] using the software (ExaVision M900, ZIOSOFT, Inc., Tokyo, Japan). Differences in assessment between observers were resolved by consensus after the images were reviewed at a separate session.

2.4. Determination of CT density in the plaque

To determine plaque configuration by MSCT, on the axial or cross-sectional MPR images, ROIs greater than 1.0 mm² were placed at eight randomly selected points on four or more different slices within the plaque area for each plaque as shown in Fig. 2 [5,6]. The CT density measurements were expressed by Hounsfield units, using the software (NIH image). Data reconstruction, detection of plaques as well as quantitative measurements were
performed and repeated several times with different reconstruction modalities by one observer who was blinded to the angiographic and ultrasonic results to account for reproducibility.

2.5. Quantitative coronary angiography

Coronary cineangiograms were recorded using a Philips cineangiographic system (Philips Medical Systems, Tokyo, Japan). Coronary angiography was performed using the Judkins technique with contrast material (Omnipaque, Daiichi Pharmaceutical Co., Tokyo, Japan). Coronary angiograms were analyzed by quantitative coronary angiography using the Cardiovascular Measurement System (CMS-MEDIS Medical Imaging Systems, Leiden, the Netherlands). Percent area stenosis and minimal lumen diameters were measured within all detectable plaques in projections showing the highest lesion severity. Lesion severity was classified as mild (50%) in the presence of <50% area stenosis, intermediate (75%) in the presence of 50–70% area stenosis, severe (90%) in the presence of 75–90% area stenosis, 95% in the presence of 90–95% area stenosis, and 99% in the presence of 95–99% area stenosis. Total occlusion was regarded as 100% area stenosis. Two cardiologist determined the degree of coronary stenosis in a separate way, without knowing the results of MSCT angiography. Differences in assessment between observers were resolved by consensus. After passage of the guidewire across the lesion, IVUS was performed after intracoronary administration of 0.2 mg nitroglycerin. Ultrasound images were obtained and the ultrasound catheter was withdrawn. The IVUS classification was performed by one observer who was blinded to the MSCT results, and it was repeated by a second independent observer to evaluate reproducibility. Plaque configuration was classified according to IVUS criteria into three groups; soft plaque, intermediate plaque and calcified plaque [7,8]. Soft plaques were defined by plaque tissue revealing an echogenicity lower than adventitia and there was no calcium detected. Calcified plaque were defined as plaque tissue containing any tissue with echogenicity as bright as or brighter than the adventitia causing acoustic shadows. Intermediate plaques were defined as plaque tissue containing any tissue with echogenicity as bright as or brighter than the adventitia and there was no calcium detected [7,8]. When classifications differed, the plaques were reevaluated until consensus between the two observers was achieved. To ensure that identical lesions were assessed by angiography and MSCT, landmarks such as the origin of sidebranches and distance to the left coronary artery ostium or bifurcation were used.

2.6. Statistics

Data are expressed as means ± SEM. Sensitivity and specificity for the detection of hemodynamically significant coronary artery stenosis were obtained using coronary artery angiogram as the golden standard. A p value of <0.05 was considered significant.

3. Results

Fifty patients (35 men) underwent both conventional and MSCT coronary angiography without major complications. Clinical characteristics of the study group are listed in Table 1. There were no reactions to contrast material and there were no adverse events. Mean age was 65 ± 9 years (ranged 43–79 years). Mean weight was 68 ± 9 kg, and mean height was 167 ± 12 cm. The imaging procedure with ECG-gated multislice CT was performed successfully in all patients. Due to the short breath-hold time, the examination was successfully completed in every patient. Homogeneous and sufficient contrast opacification of the coronary arteries was achieved in all patients, allowing visualization of not only the major coronary arteries, but also peripheral coronary artery branches.

On conventional angiography, nine patients had no significant coronary stenosis, 14 had 1-vessel disease, 16 had 2-vessel disease, and 11 had 3-vessel disease. Mean heart rate during MSCT angiography was 60 ± 8 bpm (45–74 bpm). Conventional angiography showed three significant LMT lesions, the mean interval between the two examinations was 7 ± 3 days.

Fig. 3A shows a patient in whom conventional coronary angiography diagnosed the left main trunk as normal on left caudal view (spider view). However, MSCT angiography shows us intermediate plaque in the left main trunk (Fig. 3B and C) and this was confirmed and demonstrated on IVUS (Fig. 3D).

Of 490 segments of coronary arteries, a close correlation was found between conventional CAG and MSCT angiography measurements of coronary % stenosis (Table 2). The overall sensitivity for diagnosing significant coronary stenosis was 80.2%, and the specificity was 95.6%. The positive and negative predictive values were 84.9 and 92.2%, respectively (Table 3).

The most frequent reasons for impaired evaluable motion artifacts (5 arteries), in the mid-part of the right coronary artery and the heart rate was more than 70 beats/min.

Table 1
Clinical characteristics of the study group (n = 50)

<table>
<thead>
<tr>
<th>N(%)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>65 ± 9</td>
</tr>
<tr>
<td>Male</td>
<td>35 (70%)</td>
</tr>
<tr>
<td>Female</td>
<td>15 (30%)</td>
</tr>
<tr>
<td>Smoking</td>
<td>6 (12%)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>8 (16%)</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>25 (50%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>28 (56%)</td>
</tr>
</tbody>
</table>
A total of 31 plaques were detected by both methods. On IVUS, 10 plaques were classified as soft, eight plaques as intermediate and 13 plaques as calcified. Using MSCT, soft plaques showed a mean density of $17 \pm 24$ HU, intermediate plaques $98 \pm 21$, and calcified plaques $499 \pm 192$. There were significant differences among these three groups ($p < 0.01$ ANOVA) (Fig. 4).

### Table 2
Correlation between coronary artery stenosis in MSCT angiography and coronary angiography

<table>
<thead>
<tr>
<th></th>
<th>0%</th>
<th>25%</th>
<th>50%</th>
<th>75%</th>
<th>90%</th>
<th>99%</th>
<th>100%</th>
</tr>
</thead>
<tbody>
<tr>
<td>0%</td>
<td>274</td>
<td>12</td>
<td>8</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>25%</td>
<td>46</td>
<td>22</td>
<td>6</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>74</td>
</tr>
<tr>
<td>50%</td>
<td>10</td>
<td>4</td>
<td>32</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>49</td>
</tr>
<tr>
<td>75%</td>
<td>1</td>
<td>6</td>
<td>20</td>
<td>4</td>
<td>2</td>
<td>39</td>
<td></td>
</tr>
<tr>
<td>90%</td>
<td>0</td>
<td>2</td>
<td>4</td>
<td>10</td>
<td>0</td>
<td>4</td>
<td>18</td>
</tr>
<tr>
<td>99%</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>100%</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>8</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>331</td>
</tr>
</tbody>
</table>

### Table 3
Diagnostic accuracy of multislice computed tomography

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>80.0%</td>
</tr>
<tr>
<td>Specificity</td>
<td>95.6%</td>
</tr>
<tr>
<td>PPV</td>
<td>84.9%</td>
</tr>
<tr>
<td>NNV</td>
<td>92.2%</td>
</tr>
</tbody>
</table>

**PPV**, Positive predictive value; **NNV**, Negative predictive value.

4. Discussion

Our study demonstrated that current MSCT with ECG gating allows visualization of the coronary arteries with good image quality and permits the detection of high-grade coronary artery stenosis and occlusions with high sensitivity (80.2%) and specificity (95.6%), in accordance with a previous report [9]. Moreover, plaque composition could be clearly differentiated and classified by MSCT. Good specificity suggests that MSCT may be particularly suitable for exclusion of coronary artery stenosis in patients with...
a low likelihood of coronary artery disease. And MSCT allowed visualization of coronary arteries with high image quality without admission to the hospital. And the early detection of soft plaque, which is known to be clinically important for the occurrence of acute coronary syndrome, seems to be possible.

Earlier, more active stages of coronary atherosclerosis seem more frequently associated with noncalcified or mixed plaque composition, consisting of accumulations of extracellular lipid and fibrous tissue [10,11]. This may serve to explain the results of clinical studies arguing that acute coronary syndromes occur more frequently in the absence of coronary calcium, while the presence of more extensive calcification is more characteristic of stable CAD. CT densitometry involves the measurement of attenuation values, expressed in Hounsfield units, as compared with a reference ‘phantom.’ Taniguchi et al. evaluated the accuracy of plaque density measurement within a coronary artery stenosis phantom using MSCT and assessed the influential factors [12]. He reported that plaque density is influenced by the diameter of the target vessel and the heart rate using a 0.5 mm slice, but there was no influence from the angle [12]. We used β blocker for the examination of patients with high heart rate [13, 14]. Newer generation of 16 and 64 scanner would have a potential benefits such as, better temporal resolution, fast coverage of the heart volume and high spatial resolution [13–17]. Necessity to decrease heart rate by blocker or a calcium antagonist would be mostly lost. And we could obtain images in shorter examination time and shorter breath hold time. It is expected technically that more precise evaluation of the stent lumen and more small vessels would be attained in the future.

4.1. Study limitations

Delineating soft plaque may be difficult in cases showing blurring of coronary artery edges. This is an important limitation to this technique. We did not include small plaque located in smaller coronary section. The composition of small plaque has to be elucidated by further investigation. Recent MSCT with 16 and 64 slices may allow more precise visualization of the coronary vessel wall [14–17]. Although MSCT could detect coronary artery plaque and its structure, more precise information on the plaque, such as the lipid-rich core, fibrous cap or calcified nodule is still not adequately available, these might be obtainable with advances in the technology.

5. Conclusions

MSCT for the detection of coronary artery stenosis was feasible, and plaque composition could be clearly differentiated and classified by MSCT. This is a promising method for non-invasive risk assessment in patients with known or suspected coronary artery disease.

Acknowledgements

The authors would like to thank Dr H Takashima for IVUS study, N Ushio and T Honda for expert technical assistance.

References


Shinro Matsuo MD, PhD, graduated Shiga University of Medical Science (Japan) in 1991, where he is working now in the Department of Cardiovascular and Respiratory Medicine as assistant professor. He is also a chief of cardiac imaging research. He had been clinically working as a cardiologist, mainly in cardiac imaging with nuclear cardiology and transferred his know-how to the cardiac CT. In this study, the know-how has been transferred to MSCT. The work was presented at ACC 2004 in New Orleans.

Ichiro Nakae, MD, PhD, is a cardiologist. His research interests are focused on imaging.

Tetsuya Matsumoto, MD, PhD is a cardiologist. His research interests are focused on atherosclerosis and endothelium.

Minoru Horie graduated from Kyoto University School of Medicine (Japan) in 1978. In 2002, he moved from Kyoto University to Shiga University of Medical Science as a professor of the Department of Cardiovascular and Respiratory Medicine.