Detection of Myocardial Ischemia Using 64-Slice MDCT
—— Comparison With Stress/Rest Myocardial Scintigraphy ——

Michinobu Nagao, MD; Hiroshi Matsuoka, MD*; Hideo Kawakami, MD*; Hiroshi Higashino, MD; Teruhito Mochizuki, MD; Akira Ohshita, MD*; Tamami Kohno, MD*; Susumu Shigemi, MD*

**Background:** The purpose is to investigate the ability of 64-slice multidetector computed tomography (MDCT) at rest in detecting myocardial ischemia, conventionally depicted by myocardial perfusion scintigraphy (MPS).

**Methods and Results:** In 75 patients with suspected coronary artery disease, cardiac CE-MDCT at rest and stress/rest MPS were performed. The 2D myocardial images were reconstructed in diastolic and systolic phases using raw data from coronary computed tomography (CT) angiography. CT numbers in the myocardium were used as an estimate of myocardial enhancement. The myocardium was shown using a color scale that depicts faint low-density areas more clearly than gray scale. The variation in myocardial enhancement was evaluated at systole and diastole for those segments depicted as ischemia on MPS. A pattern of transient endocardial hypoenhancement at systole and normal enhancement at diastole as the ischemic pattern on CT myocardial image was defined. MPS diagnosed myocardial ischemia in 40 of 75 patients. Use of the ischemic pattern on CT images distinguished patients with and without ischemia with a sensitivity of 90%, specificity of 83%, positive predictive value of 86% and negative predictive value of 88%.

**Conclusions:** CT myocardial imaging at rest demonstrates a characteristic enhancement pattern for ischemia. This has potential as a non-invasive method for detecting ischemia. (*Circ J* 2009; 73: 905–911)

**Key Words:** Myocardial ischemia; Myocardial scintigraphy; 64-slice MDCT

Multidetector computed tomography (MDCT) provides high-quality non-invasive images of the heart and coronary vasculature. The current-generation 64-slice scanners allow rapid scanning of the cardiac anatomy, require minimal patient cooperation and have improved image quality and high diagnostic accuracy for coronary artery stenosis.

Recent studies report that the myocardial enhancement pattern of early defect and late enhancement on 64-slice MDCT enables non-invasive assessment of myocardial viability in acute myocardial infarction.

The first-pass imaging of MDCT using pharmacological stress has recently been used to assess myocardial perfusion quantitatively; however, detection of myocardial ischemia at rest using cardiac computed tomography (CT) alone has yet to be elucidated. This is the purpose of the present study.

Several physiological studies have revealed the influence of cardiac contraction on systolic coronary flow and transmural myocardial perfusion. Microvascular resistance is affected by ischemia, with the effects most prominent in the subendocardium during systole and in the subepicardium during diastole. The capillary microvessels show a greater phasic change in microvascular resistance, which may function to maintain the capillary patency during systole.

Consequently, the increase in subendocardial resistance induced by ischemia causes a decrease in the capacitance of microvessels during systole.

In a previous study, analysis of 64-slice MDCT myocardial imaging demonstrated that the subendocardial intensity for ischemia was significantly lower than that for non-ischemia at systole, whereas there was no significant difference at diastole. The 64-slice MDCT myocardial imaging at rest revealed diminished capacitance of microvessels in the subendocardium during systole in ischemia. This result is convincing proof of the physiological rationale discussed above. Accordingly, we introduce a new method that uses high-resolution 64-slice MDCT myocardial imaging in the present study, and we investigate the performance of the new method in terms of detecting myocardial ischemia, previously depicted by stress/rest myocardial perfusion scintigraphy (MPS).

**Methods**

**Study Protocol**

The present study sample was derived from consecutive patients from March 2006 to December 2007 with suspected coronary artery disease due to typical angina or atypical angina with multiple risk factors. All patients gave their informed consent and the protocol was approved by the hospital’s Ethics Committee.

The entry criteria were as follows: (1) effort or rest stable angina (documented ST-T change on electrocardiogram (ECG), or pain relieved by administration of nitroglycerin); and (2) asymptomatic patients with a high probability of
Table 1. Characteristics of Patients With Suspected CAD

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>75</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>72±8.1 (range 51–88)</td>
<td></td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>25±3 (range 17–30)</td>
<td></td>
</tr>
<tr>
<td>Male gender</td>
<td>43 (57%)</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>44 (59%)</td>
<td></td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>34 (45%)</td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>27 (36%)</td>
<td></td>
</tr>
<tr>
<td>Family history of CAD</td>
<td>4 (5%)</td>
<td></td>
</tr>
<tr>
<td>Cigarette smoking</td>
<td>15 (20%)</td>
<td></td>
</tr>
<tr>
<td>Endstage renal disease</td>
<td>0 (0%)</td>
<td></td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>15 (20%)</td>
<td></td>
</tr>
<tr>
<td>Chess pain</td>
<td>43 (57%)</td>
<td></td>
</tr>
<tr>
<td>Dyspnea</td>
<td>14 (18%)</td>
<td></td>
</tr>
</tbody>
</table>

Table 1 lists patient characteristics.

Coronary artery disease (ie, multiple coronary risk factors) or abnormal findings on exercise ECG.

The exclusion criteria were as follows: (1) a history of myocardial infarction and/or evidence of Q waves on resting ECG, or prior revascularization; (2) unstable angina (onset of angina within 1 month, severe and worsening clinical symptoms); (3) chronic atrial fibrillation; (4) deteriorated renal function (serum creatinine >1.5 mg/dl); (5) pregnancy, hyperthyroidism or allergic reaction to contrast media; (6) severe left ventricular dysfunction (left ventricular ejection fraction <20%); (7) known history of bronchial asthma; (8) congestive heart failure of New York Heart Association class IV; (9) greater than first-degree atrio-ventricular block; (10) patients with areas of subendocardial decreased attenuation related to the early images was visually judged in each vascular territory.

Myocardial images in end-diastolic and end-systolic phases were displayed sequentially to assess myocardial perfusion and independently analyzed the SPECT images. The slices were displayed sequentially to assess myocardial perfusion in each vascular territory. The presence or absence of redistribution related to the early images was visually judged in the 4 h images, which were read as positive or negative for ischemia.

CT Myocardial Imaging

Trans-axial images were reconstructed using a slice thickness of 0.625-mm and 0.4-mm increments, optimizing the position of the reconstruction window by increments/decrements of 5% of the cardiac cycle. The volume data were transferred to a dedicated workstation (Advantage Workstation 4.2, GE Healthcare) for post-processing. A commercially available program (Cardiac IQ in Advantage Windows 4.2) was used to create long-axis and short-axis images via reconstruction with RR = 40–55% and 70–85% of the cardiac cycle to minimize motion artifacts. The majority of myocardial images were made at 40% and 75% of the RR interval for systole and diastole, respectively. Assignment of the left ventricular segments was based on the ASNC/AHA statement.

We reconstructed 2D long, vertical long and short axial myocardial images in end-diastolic and end-systolic phases using the same raw data as those used for coronary CT angiography. A previous study about the analysis of myocardial ischemia using 64-slice MDCT demonstrated that the subendocardial intensity for ischemia was significantly lower than that for non-ischemia at systole, whereas there was no significant difference at diastole. Accordingly, we defined a pattern of transient systolic hypo-enhancement in the predominant endocardium and normal perfusion at diastole as the ischemic pattern on CT myocardial images.
The myocardium was shown using a color scale that depicts faint low-density areas more clearly than gray scale. The color scales were classified into five steps using the CT number as follows: 20–40: blue; 40–60: light green; 60–80: yellow; 80–100: orange; and 100–140: red HU. The warm colors represent hyper-enhancement areas with high CT numbers, while the cold colors represent hypo-enhancement areas with low CT numbers. We identified blue areas with 20–40 HU as definite ischemia and yellow, orange and red areas with more than 80 HU as non-ischemia. The light green areas adjacent to blue areas were considered as a border zone between ischemia and non-ischemia. We evaluated the variation in myocardial enhancement at systole and diastole for segments depict as ischemia or non-ischemia using stress/rest MPS. One slice of CT myocardial imaging offers a view of systolic and diastolic phases in the same myocardial section. We moved the entire short-axis, ventricle long-axis and horizontal long-axis slices at an interval of 0.6 mm throughout the whole left ventricle.

All information on the CT myocardial images regarding patients' identification was obscured and the images were then randomized. Together, 2 cardiologists with 25 and 16 years of clinical practice and 2 radiologists with 18 and 13 years of clinical practice visually judged the myocardial enhancement. No information was revealed regarding patient treatment, and disagreements were solved through consensus. Representative CT myocardial images and stress/rest MPS images for myocardial ischemia are shown in Figures 1–4.

Analysis of Coronary CT Angiography

Coronary CT angiograms were analyzed on a workstation (Advantage Workstation 4.2, GE Healthcare) using the same data as CT myocardial imaging. Scans were analyzed through consensus from 2 observers unaware of the clinical data and blinded to the results of stress/rest MPS. A previously described 15-segment American Heart Association model of the coronary tree was employed. Each...
identified lesion was examined using maximum intensity and multiplanar reconstruction techniques along multiple longitudinal axes and transversely. Lesions were classified using the maximal luminal diameter stenosis seen in any plane. Quantitative CT angiographic analysis was performed on the most severe well-defined lesion in each segment, using a previously described digital caliper method. In the case of multiple lesions in a given segment, the segment was classified according to the worst lesion. In the case of multiple abnormal segments per artery, the vessel was classified according to the worst segment. Significant stenosis was defined as a reduction in diameter of more than 50%.

Results

Results of Stress/Rest MPS

Ischemic myocardia were diagnosed using stress/rest MPS in 40 of 75 patients. Stress/rest MPS detected 111 ischemic segments in the 40 patients. The mean value of the summed ischemic segments was 2.8 segments. Of the 111 ischemic segments, 51 (46%) were in LAD territory, 30 (27%) in LCX territory and 30 (27%) in RCA territory.

The mean CT values for the endocardium in these ischemic segments were 76.4 HU at systole and 91.4 HU at diastole. The mean CT values for the endocardium in the non-ischemic segments were 90.2 HU at systole and 90.5 HU at diastole.

Diagnostic Value of Ischemic Enhancement Pattern on CT Myocardial Imaging

The ischemic enhancement pattern on CT myocardial imaging was seen in 97 segments in 44 of 75 patients. The mean value of the summed ischemic enhancement pattern segments was 2.2 segments. Of the 97 segments with the ischemic enhancement pattern, 46 (47%) were in LAD territory, 25 (26%) in LCX territory and 26 (27%) in RCA territory.

Use of the ischemic enhancement pattern on CT myocardial imaging distinguished patients with ischemia from those without to a sensitivity of 90% (36/40), specificity of 83% (29/35), positive predictive value of 86% (36/42) and negative predictive value of 88% (29/33). Of the 4 false negative patients, stress/rest MPS detected ischemia in the basal and mid anteroseptal areas in 3 patients and in the apical inferior in one patient. Of the 6 false-positive patients, CT myocardial imaging showed the ischemic enhancement pattern.
pattern in the apical anteroseptal in 4 patient, the basal anterolateral in one patient and the mid anterior in one patient.

The ischemic enhancement pattern on CT myocardial imaging was shown in 75 of 111 (68%) ischemic segments in 36 patients with ischemia. As indicated in Table 2, there were more false negative segments in the basal parts of the left ventricle than those in the mid and apical parts. The sensitivity by segment was inferior to that by patient, especially in the basal parts of left ventricle. The ischemic enhancement pattern was seen in 37 of 51 (73%) ischemic segments in LAD territory, in 21 of 30 (70%) in LCX territory, and in 17 of 30 (57%) in RCA territory. The RCA territory had more false-negative segments than LAD and LCX territories.

**Table 2. Diagnostic Value of the Ischemic Enhancement Pattern on CT Image**

<table>
<thead>
<tr>
<th>AHA segment</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
<th>11</th>
<th>12</th>
<th>13</th>
<th>14</th>
<th>15</th>
<th>16</th>
<th>17</th>
</tr>
</thead>
<tbody>
<tr>
<td>True positive</td>
<td>4</td>
<td>3</td>
<td>1</td>
<td>4</td>
<td>7</td>
<td>2</td>
<td>8</td>
<td>12</td>
<td>6</td>
<td>7</td>
<td>8</td>
<td>2</td>
<td>7</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>False negative</td>
<td>2</td>
<td>6</td>
<td>3</td>
<td>4</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>1</td>
<td>0</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>True negative</td>
<td>69</td>
<td>66</td>
<td>71</td>
<td>66</td>
<td>62</td>
<td>68</td>
<td>63</td>
<td>61</td>
<td>68</td>
<td>65</td>
<td>65</td>
<td>72</td>
<td>63</td>
<td>69</td>
<td>71</td>
<td>73</td>
<td>74</td>
</tr>
<tr>
<td>False positive</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>3</td>
<td>5</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

CT, computed tomography; AHA, American Heart Association.

**Discussion**

We introduced a new method that uses high-spatial-resolution myocardial images with 64-slice contrast-enhanced MDCT. CT myocardial imaging is obtained from the same raw data as ordinary coronary CT angiography, and directly visualizes the variation in myocardial enhancement during the cardiac cycle at rest. In the previous study, the analysis of the endocardial intensity during a cardiac cycle suggested the characteristic enhancement pattern for ischemia is a transient systolic hypo-enhancement in predominant endocardium and normal enhancement during diastole on ischemia. Although the difference in the myocardial enhancement between ischemic and non-ischemic segments was discussed, the sensitivity and specificity of the analysis were not elucidated because of the small sample size. In the present study, we have added many non-ischemic patients and investigated the diagnostic accuracy and limitations of the method. Using CT myocardial imaging, patients were diagnosed with ischemia with a sensitivity of 90% and specificity of 83%. In addition, the ischemic enhancement pattern was seen in 65% of the territories of stenosed coronary arteries depicted in the apical anteroseptal in 4 patient, the basal anterolateral in one patient and the mid anterior in one patient.
using coronary CT angiography. CT myocardial imaging is a reliable method for detecting myocardial ischemia; it is non-invasive and avoids the additional radiation exposure or pharmacological stress associated with additional scanning.

The results of the present study indicate that rest perfusion abnormalities during systole possibly yield the same information as adenosine stress studies. This finding might have major implications for the use of cardiac CT; however, the ischemic enhancement area on CT myocardial images was smaller than the ischemic area depicted by stress/rest MPS. CT myocardial images frequently could not detect ischemia in the basal parts of the left ventricle. As indicated in Figure 3, the systolic hypo-enhancement area tended to be seen in the ischemic core, which was detected by stress/rest MPS. A widely accepted explanation for adenosine-induced ischemia is the presence of coronary steal, either inter-coronary dependent or epicardial steal from the endocardium.18 The decrease in pressure caused by a coronary stenosis results in a greater decrease in the diameter of the subendocardial arterioles than in the subepicardial arterioles; furthermore, stenosis selectively reduces the dilatory response of subendocardial arterioles.25 Consequently, an adenosine decrease occurs in the predominant subendocardial blood flow in the territory with epicardial coronary stenosis. We consider that a rest perfusion abnormality during systole may exist only in the core of the territory with epicardial coronary stenosis; therefore, the perfusion CT abnormalities underestimate the extent of ischemia depicted by stress/rest MPS. In addition, we could not accurately fuse CT myocardial and MPS images in the present study. The margins of the basal parts of the left ventricle on MPS are occasionally unclear, particularly in the anteroseptal region, because the basal parts affected by partial volume of the left ventricular cavity cause low attenuation. Therefore, we might diagnose more extensive ischemia in the basal anteroseptal region on MPS than using CT myocardial imaging. These may have been the cause of the numerous false-negative segments, especially in the basal parts of the left ventricle.

We acknowledge that its inability to assess coronary artery stenosis in the presence of severe calcification is a limitation of coronary CT angiography, even when 64-slice MDCT is used.1–3 In the present study, we could not accurately assess coronary stenosis in 15% of the patients due to severe calcifications. However, both CT myocardial imaging and stress/rest MPS accurately diagnosed ischemia in these patients, as indicated in Figure 4. The use of CT myocardial imaging provides information regarding myocardial perfusion status and ischemia in the territory of a severely calcified coronary artery. CT myocardial imaging has the potential to address the limitations of coronary CT angiography, and offers a significant advantage in elevating the diagnostic accuracy of coronary artery disease.

Study Limitations

We acknowledge the following limitations of the present study. First, motion artifact caused by myocardial wall movement occasionally occurs, especially in systole, thereby affecting the diagnostic accuracy of coronary artery stenosis! Horizontal bands caused by motion artifact were sometimes seen on cardiac CT and this decreases the intensity in the myocardium, especially in the inferior walls on the short-axis cardiac images. This may have been the cause of more false-negative segments in RCA territory than in LAD and LCX territories. We often used the long-axis myocardial images in assessing hypo-enhancement in the inferior wall because the long-axis myocardial images were little affected by the banding artifact.

Second, the myocardial intensity in the cranial portions of the left ventricle tended to be higher than those in the caudal portions. Depending on the temporal resolution of the scanner, there is usually a delay in imaging the more caudal portion of the heart. This could account for the numerous false-positive segments in the apical anterior and septal wall (Table 2). To reduce the delay in imaging, MDCT with higher temporal resolution than 64-slice should ideally be used.

Conclusions

CT myocardial imaging demonstrated a characteristic enhancement pattern for ischemia of transient systolic endocardial hypo-enhancement and normal enhancement at diastole. CT myocardial imaging has potential as a non-invasive method for detecting myocardial ischemia at rest. Cardiac CT with 64-slice MDCT has a significant advantage in assessing coronary artery disease because it enables non-invasive evaluation of both coronary artery stenosis and myocardial perfusion using the same raw data of the one modality.

References