Dual-phase multi-detector computed tomography assesses jeopardised and infarcted myocardium subtending infarct-related artery early after acute myocardial infarction

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ABSTRACT

Objectives: To investigate dual-phase multi-detector computed tomography (MDCT) for assessing extent and severity of jeopardised and infarcted myocardium subtended by infarct-related artery (IRA), and its indication for revascularisation after acute myocardial infarction (AMI).

Designs, setting and patients: Prospective, single-centre study included 107 patients with uncomplicated post-AMI 3–7 days, who met criteria and underwent dual-phase 64-slice MDCT. IRA, culprit lesion and extent of jeopardised/infarcted myocardium were assessed by three-dimensional (3D) volume-rendered images with myocardium maps and computed tomography angiography (CTA), compared with stress-redistribution thallium-201 single-photon emission computed tomography (SPECT) plus conventional coronary angiography (CCA). MDCT-jeopardised score (severity of jeopardised myocardium) was defined as extent of jeopardised myocardium multiplied by the weighted factor dependent on culprit lesion severity compared with SPECT-SRS (summation of segmental reversible score). The IRA indication for revascularisation was evaluated by MDCT-jeopardised score plus CTA. SPECT-SRS ≥2 plus CCA-culprit lesion ≥50% was the standard reference.

Results: The presence of MDCT-delayed enhancement was found in 101 (94.4%) patients. The IRA and culprit lesion were identified in 99 (92.5%) patients by MDCT-myocardium maps plus CTA. The concordance between MDCT and SPECT for detecting infarcted myocardium was good (kappa = 0.702). The correlation between MDCT-jeopardised score and SPECT-SRS was 0.741. The correlation between CTA and CCA for culprit lesion severity was 0.85. The sensitivity, specificity, negative and positive predictive values of MDCT-jeopardised score ≥2.5 plus CTA for indicating revascularisation were 90.2%, 80.4%, 86.0% and 85.9%, respectively.

Conclusions: Dual-phase MDCT has good accuracy for identifying IRA, and assessing infarcted and jeopardised myocardium for clinical relevance. It provides an alternative for triage and therapeutic planning in post-AMI.

Patients and methods

From September 2007 to August 2008, AMI patients admitted to our cardiovascular centre who did not receive primary or rescue angioplasty were evaluated to participate in this prospective study. Diagnosis of myocardial infarction (MI) was defined by typical angina lasting ≥30 minutes; biochemical evidence of peak creatine phosphokinase over twice the normal upper limit and/or new electrocardiographic (ECG) changes including development of Q wave or ST/T changes lasting 48 hours or longer. Patients were excluded if they had history of previous MI, resting angina beyond the initial 24 hours, developing functional class III or IV heart failure, cardiomyopathy, contraindication to iodated contrast agent, atrial fibrillation or serum creatinine >1.6 mg/dl. Figure 1 shows the flowchart of the study design and lists for patient ineligibility. Patients underwent MDCT and stress-redistribution SPECT protocol 3–7 days after AMI, followed by CCA within 1–2 days using standard techniques. The study was approved by our institutional review board; all participants gave written informed consent.
MDCT examination was performed with Toshiba Multi-Slice Aquilion 64 system (Toshiba Medical Systems Corporation, Otawara, Japan). β-Blockers were administered one hour before MDCT scans if heart rates were >60/min. Nitrolingual spray (2 puffs, 0.4 mg/dose; Pohl-Boskamp GmBH, Hohenlockstedt, Germany) was administered 2 minutes before scanning. For early phase images, scan parameters were 64×0.5-mm collimation, rotation time 350 ms, pitch factor 0.2–0.3, tube voltage 120 kV, tube current 400 mA (range 300–600) and ECG-triggered dose modulation. Contrast agent (iopromide; 350 mg/ml, Schering, Berlin, Germany) was injected at a flow rate of 4–5 ml/s (volume dose, 1.0 ml/kg body weight), followed by 30 ml saline solution flush, via a power injector system. Once signal intensity at the ascending aorta reached the predefined threshold of 150 Hounsfield units, the helical scan started automatically. Images were acquired during a single breath hold. After early phase acquisition, additional iopromide (0.4 ml/kg) was infused at a rate of 0.50 ml/s. Ten minutes later, late phase images were acquired. Detector collimation was increased to 1.5 mm, and tube voltage was reduced to 80–100 kV depending on patient’s body size. The effective radiation dose was estimated from the product of dose-length product times a conversion coefficient for the chest (k = 0.017 mSv.mGy⁻¹.cm⁻¹). Early phase dose was 10–15 mSv and late phase was 3–5 mSv. Raw data from the scans were reconstructed using a half-scan algorithm for patients with heart rate <65 beats/min and segmental (two or three) reconstruction algorithm for heart rate >65 beats/min.

Stress-redistribution Tl-201 SPECT data acquisition
Dipyridamole 0.56 mg/kg body weight was infused intravenously for 4 minutes with patients in a supine position. Four minutes after discontinuation, patients received 111 MBq of thallium-201 (Tl-201) intravenously. Imaging was performed using Siemens Symbia-T SPECT-CT imaging systems (Siemens Medical Solutions, Hoffman Estates, IL, USA) at 5–10 minutes and 4 hours after Tl-201 injection. Acquisition was synchronised with ECG with an acceptance window of 20%; each projection was divided into eight images per cardiac cycle. Images were acquired in a 64×64 matrix with a 1.50 acquisition zoom and reconstructed by filtered back projection with Butterworth filter with an order of 5 and critical frequency of 0.45 cycles per pixel.

MDCT image analysis
MDCT scans were evaluated using a dedicated workstation (Vitrea 2; Vital Images, Minnetonka, MI, USA). All scans were interpreted separately by two experienced reviewers blinded to patient data and SPECT results. Three steps were performed, as shown in figure 2A and B.

Step 1 for location of infarcted myocardium
Step 1 for location of infarcted myocardium was evaluated. Late phase MDCT scans were reconstructed by multiplanar reformation (MPR) and transformed into short-axis, transverse-axis and long-axis views, which were simultaneously displayed on the workstation (window-width/level 120–160/80–120 HU). The LV myocardium, divided into 17 segments as proposed by the American Heart Association, was examined for the presence of hyperenhanced regions, defined as increased signal regions with a mean difference of at least 20 Hounsfield units to differentiate infarcted from normal myocardium, measured by using regions of interest of about 20 mm² within both hyperenhanced and contiguous normal regions. Subendocardial areas of hypoenhancement within the hyperenhanced area were also considered part of the hyperenhanced area.

Step 2 assessed coronary plaque severity
Step 2 assessed coronary plaque severity (lesion stenosis and length). Following inspection of 3D volume-rendered images,
Figure 2  MDCT image analysis in a 50-year-old-man post-AMI (4 days) compared with SPECT plus conventional coronary angiography (CCA). (A) Short-axis views show delayed enhancement (DE) in the inferior-lateral wall. (B) 3D inverse angio-emulation view (left upper) and curved multiplanar reformation image (left lower) show right coronary artery (RCA) having total occlusion with contrast filling distal to occlusion (arrows); left anterior descending artery and left circumflex artery are normal. Sketches illustrate how to assess extent of infarcted/jeopardised myocardium, under 3D volume-rendered image from posterior view by a 17-segment model. Extent of infarcted/jeopardised myocardium was 5 segments (S4-5, S9-10, S15), 35.4% area was infarcted myocardium (DE was planimetered and calculated in short-axis images with 8-mm slice thickness along long-axis). The extent of jeopardised myocardium is 3.23 $= 5 \times (100\% - 35.4\%)$ and jeopardised score is 6.46. (C) SPECT images show partial reversible perfusion in S4-5, S10-11 and S15; summated reversible score is 5. (D) CCA shows RCA having total occlusion (arrow) and collateral from left coronary artery.

From the three steps mentioned, we further measured four infarct-related parameters as follows:

1. Extent of jeopardised/infarcted myocardium, which was defined as the total number of myocardial segments, semi-quantified by a 17-segment model, subending to the culprit lesion of IRA.

2. Extent of infarcted myocardium, which was defined as the total area of DE. Short-axis images (slice thickness 8 mm, slice distance 8 mm from LV outflow tract to apex on long-axis length) were used to measure DE. DE-segmental extent was manually planimetered, calculated, divided by total area of extent of jeopardised/infarcted myocardium and expressed as a percentage.

3. Extent of jeopardised myocardium, which was defined as extent of jeopardised/infarcted myocardium minus the total area with the presence of DE.

4. Jeopardised score, representing severity of jeopardised myocardium, was defined as extent of jeopardised myocardium multiplied by the weighted factor. The weighted factor is dependent on stenotic severity of culprit lesion$^{16}$ (culprit lesion $<40\%$, 0; 40–70\%, 0.5; >70–90\%, 1; >90\% stenosis with the presence of contrast filling distal to the lesion, 2; and >90\% stenosis with absence of contrast filling distal to the lesion, 1).

SPECT image analysis

Gated SPECT images of stress and redistribution studies were displayed in short-axis, long-axis and transverse-axis views and judged, in consensus, by two experienced observers blind to MDCT findings. The myocardium was divided into a 17-segment model. The myocardial region of interest with the maximum count was used as the normal reference region. Mean TI-201 activity in each segment was quantified as a proportion of maximum counts in the reference region on the image. The presence of infarcted myocardium by SPECT was defined as segments with tracer activity <75% of maximum tracer activity on redistribution images. Allocation of IRA territory was determined by segments having a presence of infarcted myocardium attributed to major coronary artery distribution. In watershed regions, allocation was determined by overlapping the maximum contour of the defect distribution. The dominance of coronary artery and its distribution by invasive CCA findings were taken into consideration. The segments were considered irreversible if segmental TI-201 activity was
unchanged or increased <10% on redistribution, compared with stress images. The segmental reversible score was defined as 1 if relative Tl-201 activity increased by ≥10%–20%, 2 if >20%–40% and 3 if >40% in the redistribution images. Summation of reversible score (SRS) in the IRA territory represented severity of jeopardised myocardium by SPECT; SRS ≥2 was considered the threshold for indicating for revascularisation.

**CCA analysis**
Coronary angiograms were analysed by two physicians blind to MDCT data. Quantitative coronary angiography was used to measure lesions with the CAAS II system (Pie Medical, Maastricht, The Netherlands). Culprit lesions by CCA criteria were determined as follows: an intraluminal filling defect consistent with thrombus, an abrupt vessel cut-off with persistence of contrast, plaque ulceration, plaque irregularity. The reference standard for the IRA/culprit lesion was based on a combination of acute ECG changes, wall-motion abnormalities on contrast ventriculography and CCA findings (coronary anatomy, lesion morphology). In addition, vessel dominance, site of the left anterior descending coronary artery (LAD) termination and infarct-related segments subtending distal to the culprit lesion were also assessed.

**Statistical analysis**
Data are presented as number (%) or mean (SD). Categorical data were compared using χ². Continuous data were compared using the Student t test. Agreement was calculated by kappa statistics. Comparison between MDCT-jeopardised score and SPECT-SRS was performed using Pearson’s regression analysis. Receiver-operating characteristic (ROC) analysis evaluated optimal cut-off value of MDCT-jeopardised score; combined with CTA, it predicted diagnostic accuracy in detecting SRS ≥2. Interobserver difference for MDCT measurements was evaluated by coefficient of variance, defined as standard deviation of absolute difference between two measurements divided by their average. A p value <0.05 was considered statistically significant. All calculations were performed using SPSS version 12.0.

**RESULTS**

**Patient characteristics**
In total, 113 patients meeting the criteria had MDCT, SPECT and CCA performed 3–7 days post-AMI. Mean (SD) heart rate was 58 (6) beats/min (range 46–72) during MDCT acquisition. Six patients were excluded owing to poor MDCT image quality (motion artefacts and/or heavy calcification). Thus, 107 patients with a mean (SD) age of 58 (12) years were analysed. Among 64 patients having ST-segment elevation on arrival, 28 (26%) received thrombolytic therapy within 12 hours after AMI attack; 36 did not, because of arrival delay. Sixty-six (62%) developed Q-wave MI after admission. Demographic characteristics are shown in table 1.

**Dual-phase MDCT findings**
In all, 185 coronary plaques with ≥50% diameter stenosis were identified by CTA alone. The presence of MDCT-DE was found in 101 (94.4%) patients. MDCT-myocardium maps plus CTA analysis accurately identified IRA and culprit lesion in 99 (92.5%) patients; additional CCA data confirmed culprit lesions in the remaining eight (six patients with absence of DE, two with double lesions showing similar plaque area and low density in the IRA). MDCT results are summarised in table 2.

**Comparing dual-phase MDCT and SPECT for assessment of jeopardised/infarcted myocardium subtended by IRA territory**
Concordance between MDCT-DE and SPECT for detecting the presence or absence of infarcted myocardium by per-segment analysis was good (kappa value 0.702). In all, 663 jeopardised/infarcted myocardial segments were identified by MDCT; as DE-segmental extent (0%, 1–25%, 26–50%, 51–75% and >75%) increased, the corresponding TI-201 uptake significantly decreased on redistribution images (p<0.001) (fig 3A).
Table 2  Dual-phase MDCT and CCA results and comparisons (n = 107)

<table>
<thead>
<tr>
<th></th>
<th>MDCT</th>
<th>CCA</th>
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<tbody>
<tr>
<td>Coronary artery anatomy</td>
<td></td>
<td></td>
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<tr>
<td>Coronary dominance</td>
<td>71/12/24</td>
<td>71/12/24</td>
</tr>
<tr>
<td>LAD terminating</td>
<td>11/42/54</td>
<td>11/43/52</td>
</tr>
<tr>
<td>Number of diseased vessel</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single-vessel disease</td>
<td>66</td>
<td>67</td>
</tr>
<tr>
<td>Two-vessel disease</td>
<td>29</td>
<td>30</td>
</tr>
<tr>
<td>Three-vessel disease</td>
<td>12</td>
<td>10</td>
</tr>
<tr>
<td>IRA/culprit lesion site*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LM</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>LAD: proximal/middle/distal/ diagonal</td>
<td>19/25/3/2</td>
<td>19/25/3/2</td>
</tr>
<tr>
<td>LCX: proximal/middle/distal/ obtuse marginal</td>
<td>6/10/8/3</td>
<td>6/10/8/3</td>
</tr>
<tr>
<td>RCA: Proximal/middle/distal</td>
<td>7/16/7</td>
<td>7/16/7</td>
</tr>
<tr>
<td>Culprit lesion measurements</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Residual diameter stenosis (%)</td>
<td>82 (18)</td>
<td>80 (20.3)</td>
</tr>
<tr>
<td>&lt;40%</td>
<td>8/20/27/29</td>
<td>8/23/26/27</td>
</tr>
<tr>
<td>40–70%</td>
<td>23.8 (7.2)</td>
<td></td>
</tr>
<tr>
<td>&gt;70–90%</td>
<td>38.5 (14.2)</td>
<td></td>
</tr>
<tr>
<td>Plaque length (mm)</td>
<td>16.1(10.2)</td>
<td>14.8 (11.1)</td>
</tr>
<tr>
<td>Plaque area (mm²)</td>
<td>23.8 (7.2)</td>
<td></td>
</tr>
<tr>
<td>Extent of jeopardised/infarcted segments</td>
<td>6.2 (2.2)</td>
<td>6.1 (2.2)</td>
</tr>
<tr>
<td>Extent of infarcted myocardium (%)</td>
<td>36.7 (32.7)</td>
<td></td>
</tr>
<tr>
<td>Extent of jeopardised myocardium (%)</td>
<td>63.3 (34.8)</td>
<td></td>
</tr>
</tbody>
</table>

Data are presented as number or mean (SD). Agreement was presented by kappa value ($\kappa$). Correlation was presented by correlation coefficient ($r$).

*IRA/culprit lesion site: see text regarding if MDCT or CCA alone was insufficiency to identify it, how to confirm them by other modalities.

CCA, conventional coronary angiography; DE, delayed enhancement; HU, Hounsfield unit; LM, left main coronary artery; LAD, left anterior descending coronary artery; LCX, left circumflex; MDCT, multi-detector computed tomography; RCA, right coronary artery.

Figure 3B shows that correlation between MDCT-jeopardised score and SPECT-SRS was 0.741 (p<0.001). Figure 4 shows ROC analysis for the extent and severity of jeopardised myocardium by our study methodology in detecting SRS >2 the areas under the ROC curve (AUC) were 0.691 (95% CI 0.60 to 0.78) and 0.877 (95% CI 0.80 to 0.93), respectively. The optimal cut-off value of MDCT-jeopardised score was 2.5. If the weighted factor of culprit severity was simply classified as 40%, 40–70% and 70% and then multiplied by extent of jeopardised myocardium, AUC was 0.822 (fig 4, JPS1 curve).

**DISCUSSION**

The prospective study focused on dual-phase MDCT-myocardium maps plus CTA to assess IRA culprit lesions and their subtending myocardium, both major determinants for guiding revascularisation and/or treatment. From these uncomplicated patients after first AMI, approximately 78% met MDCT criteria. 3D MDCT volume rendered image-guided gantry positioning system can simulate all possible angiographic views of the coronary vascular tree and LV myocardium. MDCT late-phase and early-phase images were analysed step by step, providing a high diagnostic performance (92.5%) for assessing IRA and culprit lesions, compared with SPECT plus CCA as standard reference. The relatively low performance for CCA alone for assigning IRA can be explained as follows: (1) 41 patients (38.3%) had non-Q MI, (2) CCA was performed 4–7 days post-AMI; culprit lesions would be missed by CCA criteria.

Invasive CCA can estimate the volume of myocardium subtended by a lesion if lesion location, vessel size and its dependent vascular bed are taken into consideration. Currently, MDCT-derived 3D volumetric and anatomical representations can be a non-invasive alternative. Faber et al
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Figure 4  ROC curves for comparing MDCT-diagnostic performance in detecting reversible perfusion by SPECT-SRS ≥2. JP extent of jeopardised myocardium by MDCT; JP1, JP multiplied by the weighted factor of CTA-culprit lesion (<40%; 0; 40–70%, 0.5; >70%, 1); JP2, JP multiplied by the weighted factor of CTA-culprit lesion (<40%; 0; 40–70%, 0.5; >70–90%, 1; >90–100% with distal contrast filling, 2; and 100% without distal contrast filling, 1). (AUC: JP2 vs JP, p<0.001; JP2 vs JP1, p = 0.007; JP1 vs JP, p<0.001).

Table 3  Accuracy of MDCT according to the presence and absence of SPECT-SRS ≥2 without/with corresponding significant stenoses on CCA in the infarct-related territory

<table>
<thead>
<tr>
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<th>SPECT-SRS ≥2</th>
<th>SPECT-SRS ≥2 plus CCA</th>
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<tbody>
<tr>
<td><strong>CTA (culprit lesion 50%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sensitivity</td>
<td>93.8% (60/64)</td>
<td>98.4% (60/61)</td>
</tr>
<tr>
<td>Specificity</td>
<td>18.6% (8/43)</td>
<td>23.9% (11/46)</td>
</tr>
<tr>
<td>Negative predictive value</td>
<td>66.7% (8/12)</td>
<td>91.7% (11/12)</td>
</tr>
<tr>
<td>Positive predictive value</td>
<td>63.2% (60/95)</td>
<td>63.2% (60/95)</td>
</tr>
<tr>
<td>Accuracy</td>
<td>63.6% (68/107)</td>
<td>68.2% (71/107)</td>
</tr>
<tr>
<td><strong>MDCT-jeopardised score (2.5) plus CTA (culprit lesion 50%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sensitivity</td>
<td>85.9% (55/64)</td>
<td>90.2% (55/61)</td>
</tr>
<tr>
<td>Specificity</td>
<td>79.1% (34/43)</td>
<td>80.4% (37/46)</td>
</tr>
<tr>
<td>Negative predictive value</td>
<td>79.1% (34/43)</td>
<td>86.0% (37/43)</td>
</tr>
<tr>
<td>Positive predictive value</td>
<td>85.9% (55/64)</td>
<td>85.9% (55/64)</td>
</tr>
<tr>
<td>Accuracy</td>
<td>83.2% (89/107)</td>
<td>86.0% (92/107)</td>
</tr>
</tbody>
</table>

arteries have significant lesions.24 The area is also influenced by the presence of co-dominance or multiple diseased vessels due to the balanced ischaemic effect. (3) Comparing segments by two different modalities could have some degree of misclassification and account for the imperfect association between anatomically based and physiologically based risk areas.

The functional impact of reversibility is a continuous range, but clinical decision-making is binary in distinguishing reversible from non-reversible infarct-related myocardium. In daily practice, when SPECT-SRS ≥2, CCA adds luminology information to aid planning the treatment. Like previous studies of culprit lesions evaluated by CTA alone,23 24 the diagnostic performance for IRA revascularisation is limited (table 3). However, if the extent of jeopardised myocardium and culprit lesion severity are evaluated together, the accuracy is good (86.0%). These findings suggest that dual-phase MDCT is well-suited for assessing clinical relevance post-AMI.

The drawback of radiation exposure should be considered for patients undergoing the dual-phase MDCT protocol, even though ECG-controlled tube current modulation was adopted. The estimated mean effective radiation dose in the MDCT protocol was about 14–20 mSv; this is not higher than that administered by TI-201 (around 17 mSv) plus CCA (around 4–6 mSv).27 28 The study also provides a starting point for future investigations with new scanners or techniques such as low radiation exposure using prospectively ECG triggering.29

**Limitations**

First, only uncomplicated AMI patients were included. Second, the additional injection of TI-201 was not administered when redistribution images were obtained owing to consideration of radiation exposure. This may reduce the sensitivity in detecting reversible segments. Third, we included a relatively small group. Future studies with larger populations are needed to confirm our results. Fourth, an absolute quantitative approach was not used to determine the extent of jeopardised/infarcted myocardium. Currently, the resolution of epicoronary diameter less than 1.0 mm and intra-myocardial vessel detection by 3D volume-rendered image are still limited. Therefore, it was semi-quantified by the 17-segment model, which is widely accepted in daily practice. Finally, six patients were excluded because of motion artefacts or severe calcification at the culprit lesion/non-culprit lesion segments, interfering with the accuracy of measurement. The latest generation MDCT (such as advanced dual-source MDCT) may be more suitable for these patients after AMI.

**CONCLUSIONS**

The combination of dual-phase MDCT myocardial maps plus CTA enables a non-invasive strategy for identifying IRA, assessing extent of infarcted and jeopardised myocardium and determining IRA revascularisation. It can provide an alternative choice for risk triage and therapeutic planning in selected patients after AMI (3–7 days).

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