Multidetector Row Computed Tomography Noninvasively Assesses Coronary Reperfusion After Thrombolytic Therapy in Patients With ST Elevation Myocardial Infarction

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Background The study objective was to assess the efficacy of 16-slice multidetector row computed tomography (MDCT) in estimating residual stenosis and successful reperfusion after thrombolysis in patients with ST-elevation myocardial infarction (STEMI).

Methods and Results A total of 31 patients with STEMI underwent MDCT scanning within 6 h (mean 4.6±1.1) after thrombolysis and the results for detection of significant residual stenosis and distal flow of the infarct-related artery were compared with those from conventional coronary angiography (CCAG) performed within 24 h (mean 12.1±5.6) after the MDCT scan. Successful reperfusion was defined as Thrombolysis In Myocardial Infarction flow 2 or 3 on CCAG and full contrast enhancement of the distal artery landmarks on MDCT. A final analysis was performed using 24 patients (312 segments). MDCT had a positive predictive value of 73.3% and a negative predictive value of 95.1% for detecting significant residual stenosis. It accurately estimated 17 of 18 patients (94.4%) with successful reperfusion and 5 of 6 (83.3%) with failed reperfusion on the basis of comparison with CCAG.

Conclusions MDCT demonstrated high accuracy not only for the detecting residual stenosis, but also for assessing successful reperfusion after thrombolytic therapy in patients with STEMI.

Key Words: Coronary reperfusion; Multidetector row computed tomography (MDCT); ST elevation myocardial infarction (STEMI)
therapy rather than primary percutaneous coronary intervention as the initial coronary reperfusion treatment. Patients with cardiogenic shock, atrial fibrillation or other arrhythmias, renal impairment (serum creatinine >1.5 mg/dl), known contraindications for the administration of iodine-contrast agent, or clinical signs of severe heart failure (New York Heart Association III or IV) were excluded. Other exclusion criteria were prior implantation of a coronary stent or prior coronary bypass surgery. Patients with severe coronary calcification or severe motion artifacts identified by MDCT were also excluded. We obtained the approval of the Institutional Review Board of the Catholic University of Korea and all patients gave written informed consent.

Study Design and Treatments

All patients received intravenous tenecteplase (Metylase®, Boehringer Ingelheim, Germany; 0.5 mg/kg) with intravenous infusion of conventional heparin. Patients were also given oral aspirin 100 mg and clopidogrel 75 mg daily after an initial loading dosage of 300 mg clopidogrel. Other medications such as β-blockers, angiotensin-converting enzyme inhibitors, and nitrates were also used as clinically indicated. Within 6 h of initiating thrombolytic therapy, MDCT was performed to evaluate residual coronary artery stenosis and distal flow in the IRA. In order to obtain motion-free coronary imaging, the heart rate of each patient was decreased to less than 70 beats/min by intravenous injection of a short-acting β-blocker (500 μg/kg of esmolol) just before scanning with or without 10–30 mg of oral propranolol. Conventional coronary angiography (CCAG) was carried out immediately (within at least 24 h) after MDCT scanning. Finally, we selected as subjects any patient in whom all 13 coronary segments were assessed by MDCT as without severe coronary calcification and we compared those findings to the results from CCAG. Electrocardiographic (ECG) monitoring was performed in all patients and echocardiography was done for the assessment of cardiac function and identification of left ventricular wall motion abnormality. Thus, we determined the IRA on the basis of the location of ST-segment elevation on initial ECG and location of abnormal wall motion on initial echocardiography.

Definitions and Classifications

The diagnosis of acute STEMI was made on the basis of the classical criteria4 Patients who showed ST-segment elevation ≥0.2 mV in at least 2 contiguous ECG leads, and fulfilled at least 1 of the following criteria were diagnosed with acute STEMI and included in our study. The clinical criteria included: (1) typical chest pain >30 min and (2) an elevated level of cardiac enzymes such as creatine kinase-MB and troponin.

The location of coronary stenosis was determined according to the modified American Heart Association classification.8 The right coronary artery (RCA) was divided into proximal (1), middle (2), distal segments (3), and posterior descending and posterolateral branches (4). The left main artery is noted as segment 5. The left anterior descending artery (LAD) consisted of proximal (6), middle (7), and distal segments (8) and diagonal branches (the first branch: 9, the second branch: 10). The left circumflex artery (LCX) comprised proximal (11), distal segments (12) and the first marginal branch (13).

The agatston score equivalent (ASE) was used for quantification of the coronary calcium burden and severe calcification was defined as an ASE >1,0009. Image quality of the MDCT was classified according to the criteria proposed by Kuettner et al.6 Classification of the MDCT images was defined as “excellent” (no motion artifact present), “good” (minor motion artifacts present), “moderate” (substantial motion artifacts present, but luminal assessment regarding significant stenosis still possible), “heavily calcified” (vessel lumen obscured by calcification) and “blurred” (only contrast visualization inside the vessel possible, no luminal assessment regarding significant stenosis possible). Subjects with images that could be assessed were defined as patients with “excellent”, “good” or “moderate” image quality in all 13 coronary segments.

Significant residual stenosis for each coronary segment was defined by stenosis ≥50% of the vessel diameter after thrombolysis, which included total occlusion of vessels.

MDCT Scanning

The MDCT images were acquired using a 16-detector computed tomography (CT) scanner (Sensation 16, Siemens Medical Systems, Germany). The scanning technique has been described in several previous reports.6,7,9,16 A native scan without contrast media was carried out to estimate the total calcium burden present in the coronary arteries. Scanning was performed with a 16×0.75 mm collimation, table feed 3.5 mm/rotation. A tube rotation time of 370 ms was used. The tube voltage was 120 kV, with an effective tube current-time product of 620 mAs eff. The correct scanning delay was established by measuring the CT attenuation values in the ascending aorta using the first slice after maximum contrast as circulation time. By using a remote-control automated power injector, a total of 100 ml of intravenous contrast media and a 20 ml carbolus were injected (100 ml at 4.0 ml/s). MDCT scanning began at the aortic root and was terminated at the diaphragm. For image reconstruction, the window was set to start at a 55% RR-interval for all native images, as well as the contrast-enhanced scan during a mid-to-end diastolic phase. A combination of 3-dimensional volume rendering and multiplanar reformation was applied to the reconstruction. Full reconstructions were made for the optimal phase with 0.75-mm slice thickness with 0.5-mm increments.

Interpretation of MDCT Images

Two experienced radiologists who were unaware of the
results of CCAG reviewed the MDCT images. Initially, they excluded patients with an ASE >1,000 and then selected subjects who had images that could be assessed, as defined above, and analyzed them in a blinded fashion. The results for MDCT regarding the location of significant residual stenosis and distal flow in the IRA were compared with those for CCAG. As previously mentioned, 3-dimensional volume rendering and multiplanar reformation were used for the reconstruction, but we used only the volume rendering images in the analysis.

**Conventional Invasive CCAG**

Within 24 h of MDCT scanning, CCAG was performed using the standard Judkin’s method after injecting 3,000 units of heparin. Two cardiologists participated in collecting the data-sets for CCAG. To avoid examination bias, the examiner actually performing CCAG was not explicitly informed that the patient was a subject in our study. The other examiner, who did not have the information from the MDCT results, was asked to evaluate the coronary tree by quantitative CAG analysis (QCA), and to assess the distal flow in the IRA.

**Comparison of MDCT and CCAG Images**

The comparison of the MDCT and CCAG results was carried out only in patients who did not have severe coronary calcification and who were regarded as having “assessable” MDCT images. Initially, all 13 coronary segments were evaluated for the presence or absence of significant residual stenosis, by visual inspection by 2 radiologists for MDCT and by QCA for CCAG. Next, the distal flow in the IRA was assessed using the Thrombolysis In Myocardial Infarction (TIMI) system for CCAG (we defined TIMI 0 or 1 as failed reperfusion and TIMI 2 or 3 as successful reperfusion of the IRA), and for MDCT 2 experienced radiologists assessed the enhancement of the distal artery landmarks in each epicardial coronary artery according to the definition proposed by the TIMI Group. They defined full contrast enhancement from the ostium to the distal artery landmark of the IRA as successful reperfusion.

**Statistical Analysis**

Statistical analysis was performed with SPSS (version 11.0; Chicago, IL, USA). Continuous variables are described as mean ± standard deviation and categorical variables are presented as number (n) with percentage (%). The
diagnostic accuracy was reported as sensitivity, specificity, positive predictive value and negative predictive value.

Results
During the study period, a total of 37 patients with STEMI received tenecteplase as their initial coronary reperfusion therapy. Six patients were not scanned by MDCT because they had exclusion criteria: arrhythmia (2 patients), prior coronary stent (1 patient), impaired renal function (2 patients) or patient refusal (1 patient). Thus, 31 patients with STEMI were scanned by MDCT without complications and of these, 7 patients (22.6%) were excluded because of severe coronary calcification or non-assessable images defined as “heavily calcified” or “blurred” in more than 1 coronary segment. Of these 7 patients, 3 (9.7%, 2 with “heavily calcified” and 1 with “blurred”) had non-assessable images in the IRA. Thus, the final analysis was performed for 24 patients (77.4%).

Baseline Characteristics and Quality of MDCT Images
The baseline patient characteristics are shown in Table 1. Patients arrived at hospital after 276.6±71.9 min from the onset of chest pain. The mean interval from the injection of thrombolitics to MDCT scanning was 4.6±1.1 h, and the mean interval from the MDCT scanning to CCAG was 12.1±5.6 h. Initial systolic and diastolic blood pressures were stable in all patients. On admission, the mean heart rate was relatively high at 89.1±19.5 beats/min. Twenty-three patients (95.8%) received an intravenous injection of esmolol prior to CT scanning. One patient did not receive a β-blocker because of obstructive airway disease. Thus, we obtained the correct heart rate for CT scanning (ie, 68.1±7.6 beats/min). The RCA was found to be the most frequent IRA (12 patients, 50.0%). Fifteen patients (62.5%) had diabetes.

Of the 312 segments (24 patients each with 13 coronary segments) studied, 97 had excellent image quality. There were 141 segments adjusted to good image quality, and moderate image quality was found in 74 coronary segments. The mean calcium score for the 24 patients was 348.2±124.4 ASE. Thus, our study focused on patients without severe coronary calcification and with assessable CT images.

Detection of Significant Residual Stenosis
We analyzed the location of significant residual stenosis in 312 coronary segments. CCAG detected a total of 46 segments with significant residual stenosis and MDCT correctly detected 33 (71.7%) of these segments (Fig 1). Twelve lesions were incorrectly overestimated on MDCT (stenosis ≥50% on MDCT and <50% on CCAG) and were classified as false-positive findings. Thirteen lesions underestimated on MDCT (stenosis <50% on MDCT and ≥50% on CCAG) were counted as false-negative findings. Thus, for the detection of significant residual stenosis the accuracy of MDCT was sensitivity of 71.7%, specificity of 95.5%, positive predictive value of 73.3% and negative predictive value of 95.1%.

The distribution of incorrectly assessed lesions such as false-positive and false-negative findings was also analyzed. Distal segments or side branches had 19 (76.0%) of the 25
incorrectly assessed segments (seg 3:2; seg 4:3; seg 8:3; seg 9:2; seg 10:0; seg 12:5; seg 13:4). Only 6 segments (24.0%) were proximal (seg 1:1; seg 2:1; seg 5:0; seg 6:1; seg 7:1; seg 11:2). These findings show that distal coronary segments and side branches are difficult areas for assessment by MDCT. Of these false-positive or -negative findings, the LCX accounted for 11 lesions (44.0%) and the LAD for 7 (28.0%) lesions. The remaining 7 lesions were found in the RCA. Thus, the LCX is the most difficult epicardial coronary artery for exact evaluation by MDCT.

Assessment of Reperfusion Status in the IRA

Distal flow in the IRA was evaluated by MDCT and CCAG scanning in 24 patients. CCAG identified 7 patients (29.2%) with TIMI 3 flow and 11 patients (45.8%) with TIMI 2 flow, who were considered as having successful reperfusion of the IRA. However, there were 6 patients who had failed coronary reperfusion: 1 (4.2%) with TIMI 1 flow.

Fig 3. Failed reperfusion of the infarct-related artery. (A) An abrupt cut-off point can be seen in segment 3 (arrows). Conventional coronary angiography (CCAG) shows Thrombolysis In Myocardial Infarction (TIMI) 0 distal flow (arrow). (B) Multidetector row computed tomography shows significant residual stenosis in segment 7 (circle), and the distal portion of the left anterior descending artery (LAD) tapers off with non-enhancement of the distal artery landmark (arrows). TIMI 1 distal flow in the LAD (arrows) with significant stenosis in segment 7 (circle) can be seen on CCAG.

Fig 4. False-positive finding. (A) Multidetector row computed tomography (MDCT) scanning shows an interrupted lesion in segment 7 (arrows) with enhanced distal portion of the infarct-related artery. (B) Conventional coronary angiography shows the left anterior descending artery has a total occlusion in segment 6 (circle), and a high grade of retrograde collateral flow (arrows) from the far distal portion to the point near the site of total occlusion. Distal enhancement on MDCT was visualized by this retrograde collateral flow, which we regarded as a false-positive finding.
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Circulation Journal   Vol.70, December 2006

and 5 (20.8%) with TIMI 0 flow. There were a total of 18 patients for whom MDCT identified successful reperfusion of IRA and of these, 17 had successful reperfusion (11 patients with TIMI 2 and 6 patients with TIMI 3 distal flow) on CCAG. Six patients showed failed reperfusion on MDCT and 5 of them demonstrated failed reperfusion of the IRA (4 patients with TIMI 0 and 1 patient with TIMI 1 distal flow) on CCAG. Thus, MDCT assessed correctly 17 patients with successful reperfusion (Fig 2) and 5 patients with failed reperfusion (Fig 3). Incorrect assessment of reperfusion status by MDCT occurred in 2 patients and of these 1 was a false-positive finding defined as ‘successful reperfusion on MDCT but failed reperfusion on CCAG’. MDCT scanning showed haziness and vessel wall irregularity with the presence of distal flow and this was determined to be significant coronary stenosis in segment 7. Although there was a stenosis that seemed interrupted and weak enhancement of the distal portion, the 2 examiners regarded the patient as having successful reperfusion because of the enhanced distal landmark. After 6h, however, CCAG revealed that the LAD had total occlusion of segment 6 and a high grade of retrograde collateral flow was noted from the far distal portion to the point near the site of total occlusion. This patient was the only case with failed reperfusion on CCAG which had been assessed as successful reperfusion on MDCT (Fig 4). Another patient, considered to be a false-negative finding defined as ‘failed reperfusion on MDCT but successful reperfusion on CCAG’, had unfavorable CT findings identified as significant stenosis in segment 6 with nonenhancement of the distal landmark of the LAD and an abrupt cut-off point in segment 9, which was suspected to be a total occlusion. This patient was regarded as a failed reperfusion and CCAG was carried out immediately. Although the diagonal branch in this patient was a small vessel with a 1.8 mm-reference diameter on QCA, it had normal distal flow (TIMI 3) on CCAG performed at 3h after CT scanning. The distal portion of the LAD also had a small diameter, but demonstrated successful reperfusion on CCAG (Fig 5).

Based on these findings, the accuracy of MDCT for the assessment of successful coronary reperfusion was established, with a positive predictive value of 94.4% and negative predictive value of 83.3%.

Discussion

The most important finding of this study is that the 16-slice MDCT was an effective modality for assessing coronary reperfusion of the IRA after thrombolytic therapy in patients with STEMI. Our study also demonstrated that 16-slice MDCT has a high predictive value for detecting significant residual coronary stenosis.

Detection of Significant Residual Stenosis With MDCT

Several previous studies have reported that 16-slice MDCT has a high efficacy for evaluating significant coronary stenosis. In patients with heart rates <60 beats/min only, Roper et al reported a high accuracy with 16-slice MDCT for detecting significant stenosis: sensitivity of 92%, specificity of 93%, positive predictive value of 79% and negative predictive value of 97%. The appropriate heart rate for obtaining MDCT images, without motion arti-
facts, is ≤65 beats/min and at least, it should be suppressed to less than 80 beats/min.5,9 In the present study we decreased the heart rate to less than 70 beats/min. Cademartiri et al showed high predictive values for MDCT with exclusion of coronary segments that had ≤2.0 mm diameter.23 Our study also showed the difficulty in assessing small diameter distal segments or side branches of coronary arteries. In addition to severe coronary calcification and rapid heart beat, a small vessel size is associated with unfavorable image quality and the difficulty in image interpretation with MDCT.9,21 Recently, Kuettner et al demonstrated a high accuracy of MDCT (sensitivity 72.0%, specificity 97.0%), even though their study included a wider spectrum of subjects, with more variable vessel sizes and heart rates. However, they reported a higher negative predictive value, of 99.8%, in a limited number of subjects who had low to moderate coronary calcium. Based on our results in combination with those of previous reports, MDCT is a useful modality for detecting significant coronary stenosis, following correct patient selection.

Comparison of MDCT With Classical Noninvasive Predictors for Coronary Reperfusion

Previous studies have reported on the efficacy of noninvasive clinical predictors for coronary reperfusion, but these have several limitations.1-3 Krucoff et al reported that the resolution of ST-segment elevation had only a sensitivity of 89% and a specificity of 82% for detection of IRA reperfusion.22 Other reports also reveal that ST segment improvement is associated with only an 84% probability of reperfusion.23 Furthermore, Bren et al established that although ST-segment improvement was documented more completely and rapidly in patients with reperfusion, the degree of ST change was not a sufficient parameter for guiding clinical decisions.24 Chest pain resolution or a change in cardiac markers has limitations similar to ST-segment resolution. Lemos et al evaluated chest pain resolution and the change in serum myoglobin level after thrombolysis, as well as ST-segment improvement in patients with acute STEMI, and showed that 41% of patients with chest pain resolution had less than TIMI 3 flow, which included 13% of patients with an occluded IRA. In addition, of the patients who met the reperfusion criterion for myoglobin, 36% showed less than TIMI 3 flow. Some prior studies showed that arrhythmias, such as an accelerated idioventricular rhythm, were documented in many patients, whether reperfusion occurred or not, which suggests that development of arrhythmia is not an accurate marker for evaluating coronary patency after thrombolysis.1,25 Although several recent studies have evaluated combined noninvasive markers with better results,4,26,27 they are of insufficient accuracy to guide clinical decisions about rescue coronary angioplasty.16,19

Assessment of Coronary Reperfusion Status in the IRA Using MDCT in Patients With STEMI

Because of the considerable improvement in the visualization of the coronary tree, 16-slice MDCT has been used in the evaluation of a wide spectrum of coronary artery diseases.28 However, the use of this modality for acute coronary syndrome has been limited to selected patients with non-STEMI and unstable angina pectoris.29,30 Recently, Chiou et al studied 72 STEMI cases in which MDCT was performed for the assessment of residual stenosis of IRA and reported the usefulness of MDCT in such patients.16 This was the first report that used MDCT for assessment of residual stenosis of IRA in patients with STEMI, but it included all patients admitted with STEMI whether thrombolytic therapy was performed or not. In fact, only 33% of the subjects received thrombolytic agents. In contrast to that study, we only enrolled patients who received thrombolytic therapy for coronary reperfusion, so our results were focused on assessing the coronary reperfusion status of the IRA using MDCT after thrombolytic therapy, and comparing these results with the TIMI grade on CCAG. In most patients, estimation of the coronary reperfusion status of the IRA was possible by MDCT scanning without any complications. Maintenance of the appropriate heart rate was easily achieved. These findings emphasize the great value of MDCT as a promising screening modality that could be used in patients with STEMI, despite its limitations in the presence of collateral flow and small vessel size.

In conclusion, 16-slice MDCT demonstrated high accuracy not only in detecting significant residual stenosis, but also in assessing successful reperfusion of the IRA after thrombolytic therapy in patients with STEMI. In the future, MDCT may play an important role in guiding further management after thrombolytic therapy.

Study Limitations

The most important limitation of this study is the relatively small number of patients. Another limitation is the high radiation exposure of approximately 5–10 mSv as well as the large volume of contrast media required for 16-slice MDCT scanning; these issues were not considered in the conclusions of this study. In general, the radiation exposure in standard diagnostic coronary angiography does not exceed 12.5 mSv.6,33 Our results demonstrating the usefulness of MDCT as a screening modality for assessing coronary reperfusion should be generally accepted for clinical application only when the safety of MDCT technology is also demonstrated. Finally, differentiation of complete occlusion and incomplete occlusion by MDCT can be a challenge, particularly when the subject has a complete occlusion with high-grade retrograde collateral flow. As shown in Fig 4, complete coronary artery occlusion with retrograde contrast opacification via collateral channels might be judged as successful reperfusion on MDCT. In this case, it could be possible that the retrograde collateral flow was demonstrated through more delayed phase of MDCT, and it could also be possible that the vein overlapped in that phase. Unfortunately, however, our MDCT scanning did not show such findings under routine conditions. This problem should be resolved by mechanical and technical developments of MDCT scanning in the near future.

Acknowledgments

We acknowledge the helpful comments of every member of the Departments of Internal Medicine and Radiology, the Catholic University of Korea.

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