

The Diagnostic Accuracy of the 64-slice Multi-detector CT Coronary Angiography for the Assessment of Coronary Artery Stenosis in Symptomatic Patients¹

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Purpose: We evaluated the diagnostic accuracy of a 64-slice multi-detector CT (MDCT) coronary angiography against a conventional coronary angiography (CCA) for the detection of significant stenosis (≥ 50% lumen diameter narrowing).

Materials and Methods: Sixty-four patients underwent a MDCT and a subsequent CCA to evaluate the presence of atypical chest pain or suspected coronary artery disease (CAD). A MDCT angiography was performed using a 64-slice MDCT-scanner (Sensation 64, slice collimation 32 × 0.6 mm). The coronary artery segments were classified according to a 15-segment model. The sensitivity, specificity, and diagnostic accuracy of the 64-slice MDCT for the detection or exclusion of significant CAD were calculated on a per-segment and per-patient basis.

Results: Fifty-nine of the 64 (92%) coronary CT angiograms were of diagnostic image quality with 93.5% (809 of 865) of the coronary segments assessable by CT angiography. One-hundred two (12.6%) segments showed significant stenosis by CCA. Stenosis of 50% or greater was detected by sensitivity, specificity, accuracy, positive predictive value, and negative predictive value on a per segment basis (89%, 99%, 97%, 90%, and 98%, respectively) and a per-patient basis (96%, 69%, 90%, 92%, and 82%, respectively).

Conclusion: The 64-slice MDCT coronary angiography demonstrated a high diagnostic accuracy for both the per-segment and per-patient analyses for this symptomatic patient group.

Index words : Computed tomography (CT)
Coronary angiography
Coronary vessels, CT
Coronary vessels, stenosis or obstruction

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Received August 18, 2008 ; Accepted August 27, 2008

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To date, the conventional coronary angiography (CCA) has been the only method used to directly visualize coronary arteries and has been the gold standard for the detection of significant coronary artery disease (CAD). However, the CCA is invasive, costly, and involves some degree of patient risk. Moreover, two-thirds of all CCAs have been performed for the diagnosis of significant stenosis without intervention (1). Recently, the use of a multi-detector CT (MDCT) coronary angiography has been rapidly evolving as a promising non-invasive method for the assessment of patients with CAD (2 - 5). The results of 16-slice MDCT coronary angiography studies have been promising; however, a number of limitations remain including the inability to assess small coronary segments (diameter < 2 mm), cardiac motion artifacts, breathing artifacts, the influence of heavily calcified vessel walls, and a low contrast-to-noise ratio (6 - 9). Similarly, the use of a 64-slice MDCT is also subject to similar limitations (10, 11). Most of the published studies on 64-slice MDCT coronary angiographies showed high sensitivity and specificity (> 90%), and a high negative predictive value (~98%), compared to the CCA in well selected and well prepared patients (12, 13). Even though the 64-slice MDCT-scanner has been widely used for the evaluation of CAD in Korea, no study has been published on the the diagnostic performance of this procedure to detect or rule out significant coronary stenosis (> 50% lumen diameter narrowing) at the Journal of Korean Radiological Society. The aim of this study was to retrospectively evaluate the diagnostic accuracy of the 64-slice MDCT coronary angiography compared with the currently used CCA for the detection of significant coronary stenosis in patients with atypical chest pain or suspected CAD.

Materials and Methods

Patient population

Among the 515 patients who visited the chest pain clinic and underwent a 64-slice MDCT to evaluate symptomatic angina with suspected CAD or atypical chest pain between October 2006 and April 2007, 64 patients (38 males, 26 females; mean age, 59 ± 8 years; range, 41 - 78 years) who also underwent a subsequent CCA were retrospectively identified for inclusion in our study. The average time between the two examinations was 14 days (range: 1 - 32 days). The exclusion criteria for the CT were included: unstable clinical condition, previous allergy to iodinated contrast agents, persistent

arrhythmias, previous coronary artery bypass graft surgery or percutaneous coronary intervention with stent implantation, elevated serum creatinine levels (> 1.5 mg/dL), and the inability to hold their breath for 15 seconds. Patients with previously positive, but untreated CCA were also excluded from the study to avoid the bias of evaluation since CAD has already been diagnosed. Figure 1 shows a flow chart of our diagnostic procedure for evaluating symptomatic patients with suspected CAD or atypical chest pain.

MDCT scanning protocol and reconstruction

Prior to the MDCT, the heart rate (HR) of each patient was measured. Patients with a pre-scanned HR > 65 beats per minute (bpm) were given an oral dose of atenolol (25 - 50 mg) one hour before the scan. All patients received nitroglycerin (0.6 mg) sublingually one minute before the MDCT to dilate the coronary arteries.

A MDCT angiography was performed using a 64-slice MDCT-scanner (Sensation 64, Siemens Medical Solutions, Forchheim, Germany). The scan parameters were as follows: slice collimation 32×0.6 mm, rotation time 0.33 ms, tube voltage 120 kV, tube current (effective mAs) 900 mA, and pitch 0.2 (3.84 mm table feed per tube rotation). The scan time was about 10 seconds in a single breath-hold. No ECG-dependent dose modulation technique was applied. The CT angiography was triggered automatically with the arrival of a main contrast bolus (automatic bolus tracking). A prescan was taken at the level of the aortic root and a region of interest (ROI) was identified on the ascending aorta. As soon as the signal density level in the ascending aorta reached a predefined threshold of 130 Hounsfield units (HU), the scan was started. We injected 70 - 80 mL non-ionic contrast media (Iomeron 400, iomeprol, 400 mg/mL, Bracco, Milan, Italy) at a flow rate of 5.0 mL/s. This was followed by a 50 mL saline chaser bolus at a flow rate of 5 mL/s to washout the contrast agent from the right ventricle. During the scan, an ECG was recorded simultaneously. The data sets were reconstructed during the mid-to-end diastolic phase, with reconstruction windows set at - 300 ms to - 450 ms before the next R-wave or 60% to 70% of the R-R interval. When an insufficient image quality was obtained, additional reconstructions during the end-systolic phase (25% to 35% of the R-R interval) were performed. For the reconstruction of axial images, we used a slice thickness of 0.75 mm and a slice width of 0.4 mm. Smooth soft-tissue reconstruction kernels (B25f) were used for reconstruction.

MDCT image analysis

All CT images were analyzed by a radiologist with at least 5 years of experience in assessing coronary CT angiography imaging. Moreover, the radiologist was blinded to the CCA findings. Segments were identified as having coronary artery stenosis as per the 15-segment American Heart Association model (14). The image evaluation was performed on a three-dimensional viewing-enabled workstation (Leonardo, Siemens Medical Solutions, Forchheim, Germany). For the evaluation of coronary artery stenosis, axial images, curved multiplanar reformations (MPR), maximum intensity projections (MIP) and volume-rendered images (VR) were employed. In particular, the lesion severity of CT-depicted stenosis was assessed with the aid of dedicated cardiac CT visualization software (Circulation, Siemens Medical Solutions, Forchheim, Germany) that extracts the course of the coronary arteries from the contrast-enhanced data set and automatically displays the vessel as a curved MPR along the centerline of the vessel. With this tool, the degree of stenosis was evaluated by applying a semi-automated distance-measuring tool to the automatically generated curved MPRs. Lesions with a diameter reduction of 50% or more were considered to have significant stenosis.

All coronary segments were included in the analysis. The calcified plaques were classified as mild to moderate (defined as small and isolated or eccentric high-den-

sity lesions in the coronary artery wall, occupying a vessel lumen < 50%) or heavy calcifications (defined as large nodular high density lesions or diffuse large high-density lesions extending longitudinally along the wall, occupying a vessel lumen ≥ 50%). Mild to moderate calcification was considered to be a low risk for significant coronary stenosis. However, a heavily calcified segment was considered as a significant lesion since the determination of an accurate degree of stenosis in the lesion was impossible due to the blooming artifact. Motion artifacts were defined as any impairment of image quality due such factors as residual cardiac motion, voluntary patient movement, or inability of patients to hold their breath, which resulted in blurred or double vessel contours. The image quality was evaluated on a per-segment basis and was classified as good (optimal depiction of the coronary arteries and the absence of image-degrading artifacts related to motion, calcification or noise), adequate (presence of artifacts but images still suitable for diagnostic purposes) or poor (data not adequate for diagnostic assessment). The reasons for poor image quality included calcifications of the vessel wall, motion artifacts, and poor contrast opacification. Segments that were of poor image quality were considered to be unevaluable.

Conventional coronary angiography

A CCA (Allura Xper FD-10, Philips Medical Systems,

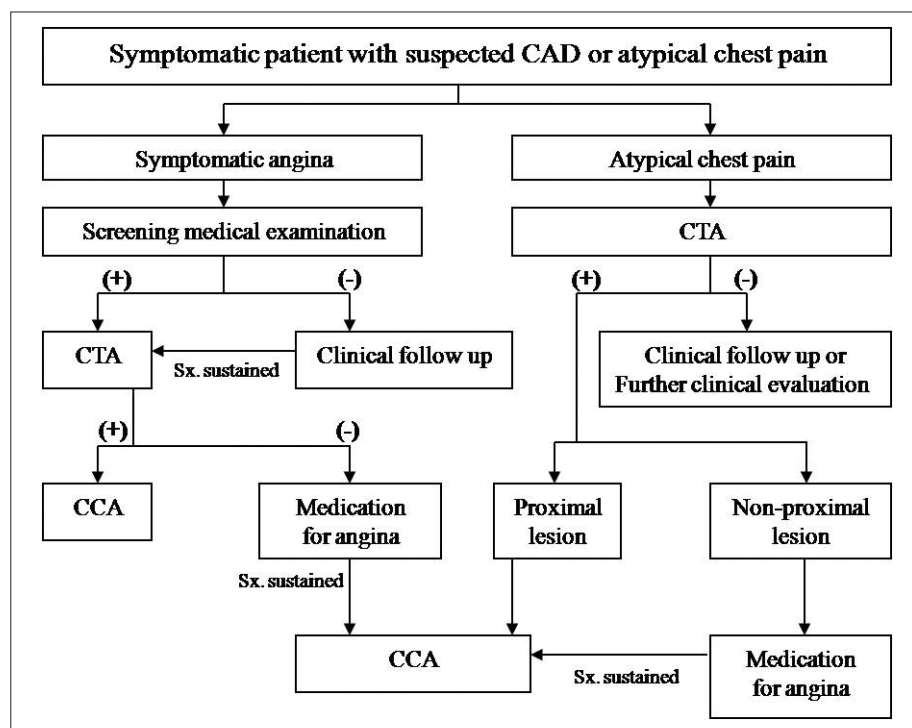


Fig. 1. Flow chart of our diagnostic procedure for evaluating a symptomatic patient with suspected coronary artery disease or atypical chest pain. CAD: coronary artery disease; CCA: conventional coronary angiography; CTA: CT angiography; Sx: symptom

Eindhoven, Netherlands) was performed within 2 - 14 days after a MDCT examination, via the femoral or radial approach. Four-French catheters and 80 - 100 mL of non-ionic contrast material (Visipaque 320, iodixanol, 320 mg I/mL, GE Healthcare, Princeton, NJ) were used. A minimum of 6 projections were obtained: 4 views of the left and 2 of the right coronary artery. All coronary segments visualized at catheterization were included for comparison with the 64-slice MDCT. The segments were classified according to the 15-segment American Heart Association model. A quantitative assessment of stenosis severity on the angiograms was performed with a stenosis grading tool and automated distance and scale distance (CAAS, Pie Medical, Maastricht, the Netherlands). The projection with the most severe degree of stenosis was used for evaluation. Significant stenosis of the coronary artery was defined as 50% luminal narrowing compared to the expected diameter of the vessels in two orthogonal projections.

Statistical analysis

With CCA as the standard of reference, the diagnostic accuracy of a CT coronary angiography for the detection of hemodynamically significant stenoses in the coronary arteries is expressed in terms of the sensitivity, specificity, accuracy, positive predictive value (PPV), and negative predictive value (NPV). The diagnostic performance

was calculated based on a per-segment and per-patient basis. The segment-based analysis included all evaluable and nonevaluable segments that were censored as positive or excluded as nonevaluable segments. True positives were defined as correct identification by a CT coronary angiography of segments with a diameter reduction of 50% or more. The patient-based analysis included all patients, and sanctioning any nonevaluable coronary segments by CT angiography as positive, while taking into consideration that this finding, would also lead to CCA in clinical practice. For the patient-based analysis, a true positive was defined as having at least one positive segment by both modalities, regardless of location.

Results

Fifty-nine (92%) of the 64 CT angiographies performed were of diagnostic image quality (image quality: 65.5% good, 26.5% moderate, and 8% poor). The reasons for the CT angiographies with poor image quality included tachyarrhythmia ($n = 3$) and extensive calcification of the vessel wall of all coronary segments ($n = 2$). Cardiovascular risk factors for the 59 patients with CT angiographies of diagnostic image quality included smoking (27 of 59; 46%), hypertension (24 of 59; 41%), diabetes (16 of 59; 27%), hyperlipidemia (13 of 59; 22%),

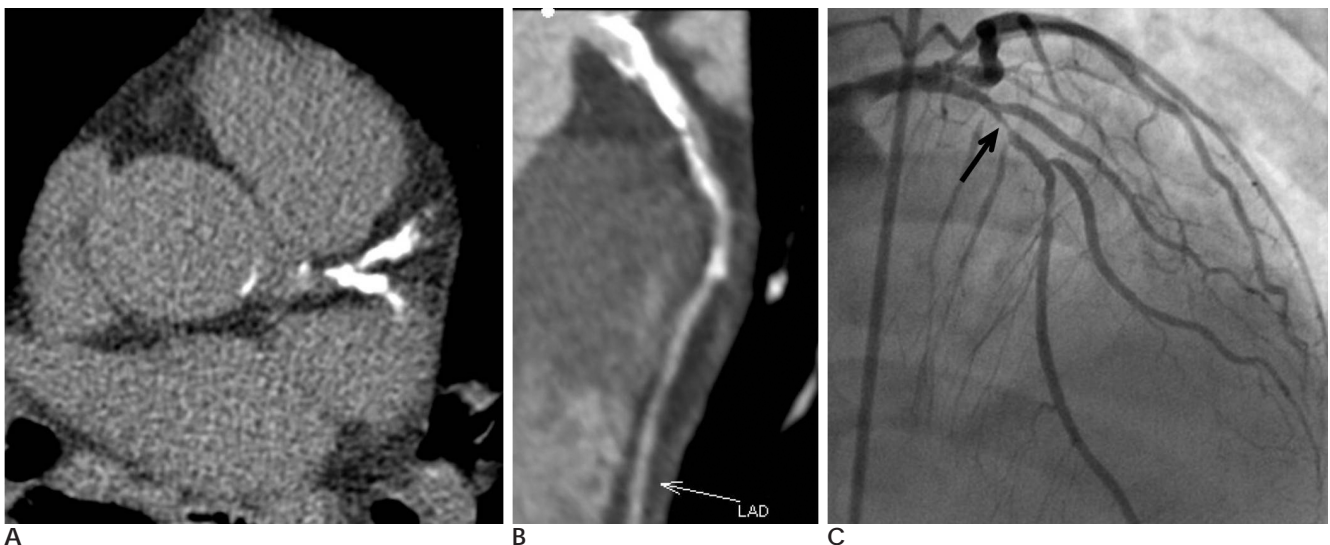


Fig. 2. A 74-year-old man with anterior chest pain over the past 2 weeks.

A. A coronary calcium scan shows calcification in the left anterior descending coronary artery (LAD) and left circumflex artery with an Agatston score of 1,088.

B. A curved multiplanar reformation of the LAD shows extensive calcification in the left main artery and proximal segment of the LAD. Excessive calcification of the vessel wall impairs accurate detection or localization of stenosis.

C. The conventional coronary angiography in the antero-posterior cranial projection confirms stenosis of the LAD (arrow) with 80% diameter reduction.

family history (10 of 59; 17%). Moreover, 41 patients (69%) presented with symptomatic angina and 18 patients (31%) presented with atypical chest pain. Oral atenolol was administered in 79% (46/59) of patients. The mean heart rate during the MDCT was 63 ± 9 bpm (range, 52 - 84 bpm). The average decrease in HR in the patients was 11 bpm when compared to the baseline HR

after administering atenolol (25 - 50 mg). Furthermore, the average Agatston calcium score was 285 ± 499 . The estimated mean radiation exposure for the contrast-enhanced MDCT scan was 15.3 ± 1.3 mSv.

Of the 885 coronary segments examined (15 segments per patient, 59 patients), 76 (8.6%) were excluded from the analysis. Reasons for exclusion included the true ab-



Fig. 3. A 62-year-old man with anterior chest pain over the last 10 days.

A. A volume-rendered image shows a significant lesion (arrow) located at the proximal segment of the LAD.

B. A curved multiplanar reformation of the LAD shows a non-calcified plaque-causing significant stenosis (arrow).

C. A conventional coronary angiography in the right antero-oblique cranial projection confirms stenosis of the LAD (arrow) with 85% diameter reduction.

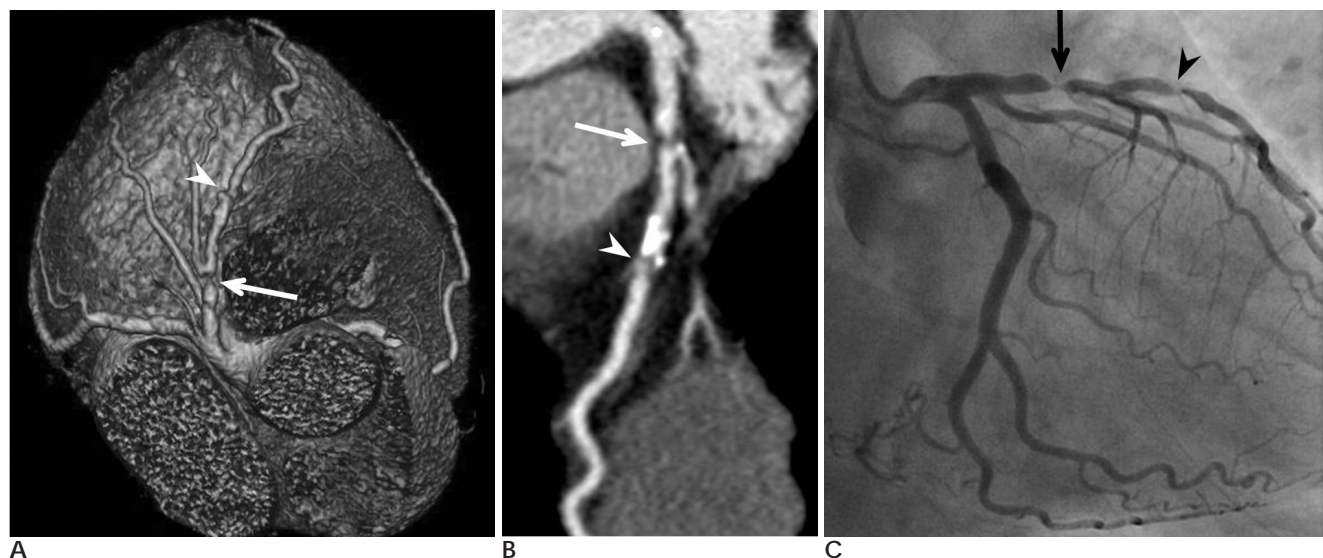


Fig. 4. A 45-year-old man with anterior chest pain over the last month.

(A) Volume-rendered and (B) curved multiplanar reformation images show significant stenosis in the proximal segment of the LAD (arrows). The middle segment of the LAD (arrowheads) was not considered as significant stenosis, but was associated with the blooming and beam-hardening artifacts of heavily calcified plaque.

(C) Conventional coronary angiography in right antero-oblique cranial projection confirmed stenoses of the proximal (arrow) and middle segments (arrowhead) of the LAD with 90% diameter reduction.

sence of vessel segment ($n = 20$) and nonevaluable segments ($n = 56$) by MDCT due to small vessel size ($n = 20$), heavy calcification ($n = 15$) (Fig. 2), poor contrast opacification ($n = 12$), and cardiac motion artifacts ($n = 9$). For the remaining 809 segments, a CCA showed 102 (12.6%) significantly stenotic segments in 78% (46/59) of patients (Fig. 3). Eighteen (30%) patients had 1-vessel disease, 20 (34%) had 2-vessel disease and eight (14%) had 3-vessel disease. A CT angiography correctly identified 91 diseased segments. Of the 56 segments nonevaluable by MDCT, 8 (14%) were significantly stenotic at CCA. Moreover, 11 were false-negative segments associated with calcified plaques ($n = 4$), poor contrast enhancement ($n = 3$), cardiac motion ($n = 2$),

measurement error ($n = 1$), and detection error ($n = 1$). On the other hand, 10 false-positive segments were identified, which were associated with calcified plaques ($n = 5$) (Fig. 4), poor contrast enhancement ($n = 2$) (Fig. 5), cardiac motion ($n = 2$), and measurement error ($n = 1$) (Fig. 6).

The sensitivity, specificity, accuracy, PPV and NPV of the 64-slice MDCT in the detection of significant coronary artery stenoses were 89%, 99%, 97%, 90% and 98%, respectively. For a patient-based analysis, the sensitivity for detecting patients with at least one positive segment, the specificity, accuracy, PPV, and NPV were 96%, 69%, 90%, 92%, and 82%, respectively. After censoring 56 nonevaluable segments as positive, segment-

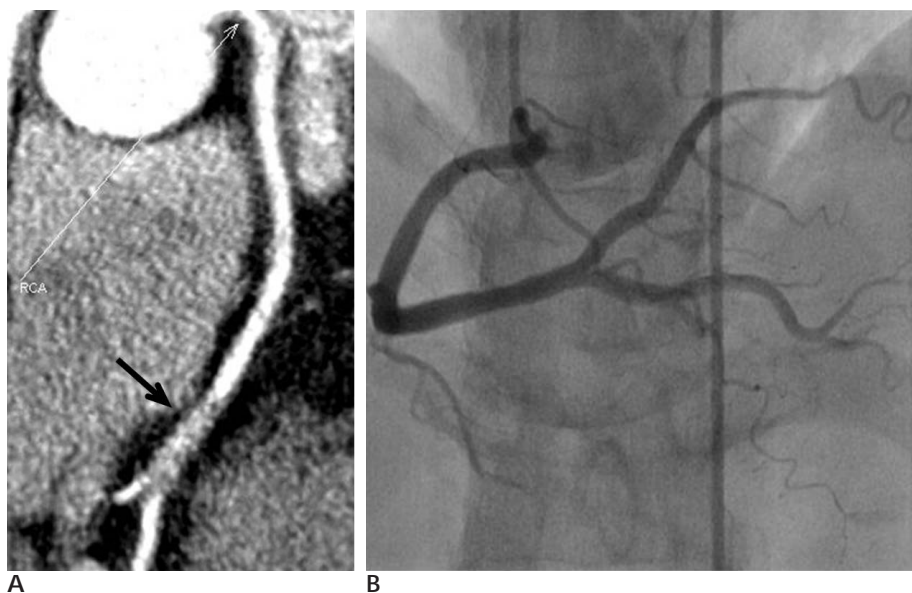


Fig. 5. A 55-year-old man with atypical chest pain over the last 4 months.

(A) A curved multiplanar reformation image shows nearly total occlusion with non-calcified plaques in the distal right coronary artery (RCA) (arrow). However, there is no stenosis in the distal RCA as seen on (B) the conventional angiography in the antero-posterior cranial projection. This misdiagnosis is considered to be associated with poor contrast opacification.

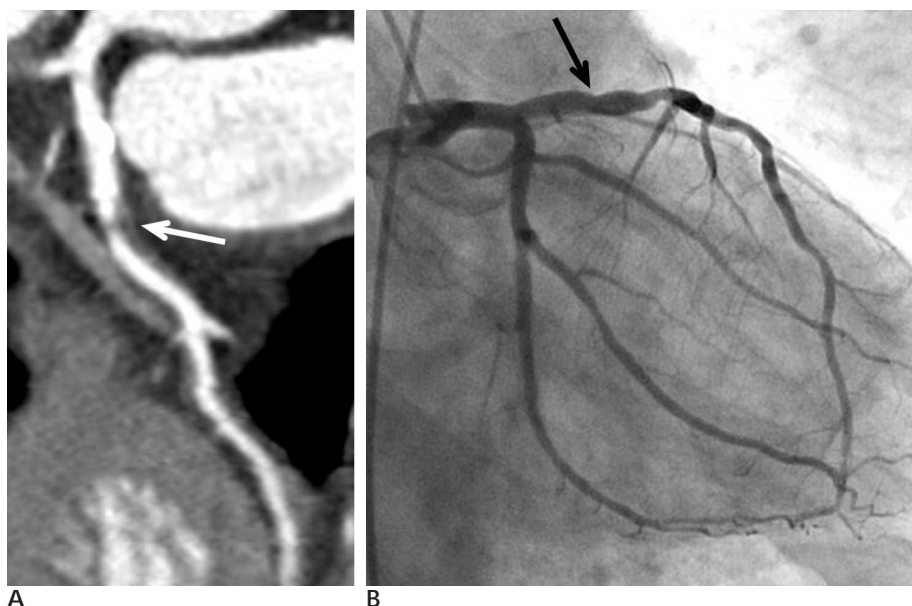


Fig. 6. A 53-year-old man with anterior chest pain over the last month.

(A) A curved multiplanar reformation image shows 55% stenosis in the middle segment of the left anterior descending coronary artery (arrow), however (B) a conventional coronary angiography in the right antero-oblique cranial projection shows a 30% diameter stenosis in the corresponding segment. This case is an example of measurement error with a stenosis-grading software tool.

Table 1. Accuracy Parameters for Segment-based and Patient-based Detection of Greater than 50% Coronary Stenosis

	All Segments for Analysis With Nonevaluable Segments "Positive" (n = 865) *	Segments for Analysis Only (n = 809) †	All Patients for Analysis and Patients With Nonevaluable Segments "Positive" (n = 59)	Patients for Analysis Only (n = 59) ‡
Stenoses by CCA (N)	110	102	46	46
Stenoses by MDCT (N)	147	91	53	48
False-positive (N)	58	10	8	4
False-negative (N)	11	11	1	2
Sensitivity (%)	90	89	98	96
Specificity (%)	92	99	38	69
Accuracy (%)	92	97	85	90
Positive predictive value (%)	63	90	85	92
Negative predictive value (%)	98	98	83	82

Abbreviations: CCA, conventional coronary angiography; MDCT, multi-detector CT.

*Excludes 20 of 885 segments that were truly absent.

†Excludes 56 of 865 segments considered non-evaluable.

‡Excludes non-evaluable segments in the counts of stenosis by MDCT.

based (patient-based) analysis revealed a sensitivity of 90%(98%), specificity of 92%(38%), accuracy of 92%(85%), PPV of 63%(85%), and NPV of 98%(83%) (Table 1).

Discussion

With the advent of the 64-slice MDCT scanner, both temporal and spatial resolutions of the coronary CT angiography have further improved for the non-invasive detection of coronary stenoses. The diagnostic performance assessment of the CAD has significantly improved, whereas the nonassessable proportion of segments has significantly decreased with the newer generations of MDCT scanners (10 - 13, 15). A recently published meta-analysis (15) has reported a high diagnostic accuracy for the 64-slice MDCT in the detection of significant stenosis on both a per patient (99% sensitivity and 93% specificity) and per segment basis (93% sensitivity and 96% specificity). The NPV for the classification of segments and patients with or without CAD was high (97 - 100%) for the published studies (10 - 13, 15, 16). Consistently, the results of our study have demonstrated that a 64-slice MDCT coronary angiography enables the detection of significant coronary stenoses with high sensitivity and specificity.

In our study, misinterpretation of coronary segments with significant image artifacts was the most important cause of false-positive and false-negative results. Heavy calcification of vessel walls is a well-known major limitation of the CT angiography (9, 17) and was the main reason for both false positive and false negative CT results (43%) in this study. Heavy calcification of a coro-

nary segment leads to overestimation of the stenosis degree in the lesion due to calcium blooming and blurring of the vessel lumen. Cardiac motion artifacts deteriorate the image quality of a CT data set. Even though beta-blockers were used to decrease the heart rate below 65 bpm, 15 patients had a heart rate above 65 bpm. A higher heart rate caused 9 segments to be excluded from further analysis. In addition, 4 segments were either underestimated or overestimated due to blurring and double contouring of a vessel with a heart rate greater than 75 bpm. A lower heart rate (< 65 bpm) and the choice of a proper reconstruction window permitted excellent visualization of both the coronary artery lumen and wall (18). Small vessel size was the main reason for exclusion of stenosis assessment in this study. However, stenoses in vessel segments with a diameter of 1.5 mm rarely constitute targets for revascularization therapy. This may imply that vessel segments > 1.5 mm diameter are clinically worthwhile (5, 19, 20). Sub-optimal vascular enhancement causes poor visibility and blurring of the vessel contour and remains a challenge to accurately determine the presence of significant stenosis; specifically in the distal vessels. Marked deterioration of image quality by poor contrast opacification was substantially more frequently observed in our study, even though we injected 70 - 80 mL of a high concentration, non-ionic contrast media at a flow rate of 5.0 mL/s using a bolus tracking method and a biphasic injection protocol. The concentration, volume and injection rate of the contrast agent must be optimized into dedicated injection protocols for a successful coronary CT angiography (21 - 23).

We used a dedicated cardiac CT visualization software (Circulation; Siemens Medical Solutions, Forchheim,

Germany) for assessing the severity of CT-depicted stenosis. One stenotic segment was overestimated and one segment was underestimated when compared with the CCA results. The difference in quantitative measurement between the use of CT angiography and CCA might result from the image quality and spatial resolution of the original acquisition (21). A CT angiography is known to be more sensitive and accurate for the detection of atherosclerotic vessel wall changes than CCA. In this respect, CCA might not be the optimal reference standard technique in all cases (12, 24). In our study, 56 (6.5%) of the 865 segments evaluated, were deemed to be nonevaluable by MDCT due to small vessel size, heavy calcification, poor contrast opacification, and cardiac motion artifact. Recent studies (10, 25) on 64-slice MDCT coronary angiographies have reported that on average, 11% of segments had to be excluded from segment-based analysis because they were deemed to be nonevaluable despite the improvement of spatial and temporal resolution of the 64-slice MDCT scanner. The high number of nonevaluable segments may lead to a high number of diagnostic CCA examinations if the 64-slice MDCT coronary angiography is used indiscriminately for excluding the presence of significant stenosis in clinical practice. In summary, the 64-slice MDCT coronary angiography is a useful noninvasive diagnostic tool for detecting significant coronary stenoses at an acceptable level of accuracy for both segment-based analyses under appropriate heart control, optimal contrast enhancement, and with the absence of extensive calcification.

In the present study, which included 59 patients with a very high prevalence of significant CAD (78%), the patient-based analysis showed a high sensitivity (96%), PPV (92%), and NPV (82%) when unevaluable segments were excluded from the analysis. The specificity on a per-patient basis was somewhat reduced (69%) as the 64-slice MDCT coronary angiography may overestimate the presence of disease. Considering that it is more important to detect significantly diseased patients reliably and send them for CCA than not to miss stenotic vessels, the moderate specificity of the MDCT for the per-patient-based analysis might be acceptable (13).

The limitations of this study include the fact that only one radiologist evaluated all the MDCT data sets and interobserver variability was not assessed even though interobserver variability is known to be low as reported in previous studies. In addition, patient sample size was relatively small. The spatial resolution of the 64-slice

MDCT scanner is still not adequate enough to identify stenoses in small vessel segments reliably. Our 64-slice MDCT scanner with 0.6-mm collimation and double z-sampling technique is expected to be vulnerable to heart rate variability due to a rather long scanning time of about 10 sec compared with those of about 6 sec for other 64-slice MDCT scanners (26). Of the 865 segments, 56 (6.5%) were nonevaluable by MDCT. The PPV on a per-segment basis and the specificity on a per-patient basis were reduced from 90% to 63% and from 69% to 38%, respectively when the nonevaluable segments were included in the analysis. Finally, the radiation exposure of the applied protocol is still considerably high.

In conclusion, the use of the 64-slice MDCT coronary angiography showed a high diagnostic accuracy on both a per-patient and per-segment analyses in this symptomatic patient group.

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