

Improved Diagnostic Accuracy With 16-Row Multi-Slice Computed Tomography Coronary Angiography

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- OBJECTIVES** We sought to compare the diagnostic value of multi-slice computed tomography (MSCT) coronary angiography (CA) to detect significant stenoses ($\geq 50\%$ lumen diameter reduction) with that of invasive CA.
- BACKGROUND** The latest 16-row MSCT scanner has a faster rotation time (375 ms) and permits scanning with a higher X-ray tube current (500 to 600 mA) during MSCT CA when compared with previous scanners.
- METHODS** We studied 51 patients (37 men, mean age 58.9 ± 10.0 years) with stable angina or atypical chest pain. Patients with pre-scan heart rates ≥ 70 beats/min received oral beta-blockade. The heart was scanned after intravenous injection of 100 ml contrast (iodine content, 400 mg/ml). Mean scan time was 18.9 ± 1.0 s. The MSCT scans were analyzed by two observers unaware of the results of invasive angiography, and all available coronary branches ≥ 2 mm were included.
- RESULTS** Invasive CA demonstrated normal arteries in 16% (8 of 51), non-significant disease in 21% (11 of 51), single-vessel disease in 37% (19 of 51), and multi-vessel disease in 26% (13 of 51) of patients. There were 64 significant lesions. Sensitivity, specificity, and positive and negative predictive values for detection of significant lesions on a segment-based analysis were 95% (61 of 64, 95% confidence interval [CI] 86 to 99), 98% (537 of 546, 95% CI 96 to 99), 87% (61 of 70, 95% CI 76 to 98), and 99% (537 of 540, 95% CI 98 to 99), respectively. All patients with angiographically normal coronary arteries or significant lesions were correctly identified. Three of 11 patients with $< 50\%$ lesions were incorrectly classified as having single-vessel disease.
- CONCLUSIONS** The 16-row MSCT CA reliably detects significant coronary stenoses in patients with atypical chest pain or stable angina pectoris. (J Am Coll Cardiol 2005;45:128–32) © 2005 by the American College of Cardiology Foundation

Ongoing advances in multi-slice computed tomography (MSCT) technology in recent years prompted us to re-evaluate the clinical potential of noninvasive coronary angiography (CA) (1–9). The latest generation of 16-row MSCT scanners have a faster X-ray tube rotation speed that provides higher temporal resolution. In addition, a higher tube current during MSCT CA can be selected, which increases the contrast-to-noise ratio and improves image quality. We report the current diagnostic performance of MSCT CA to detect significant stenoses in stable patients referred for conventional angiography on an outpatient basis.

METHODS

Study population. During a period of 7 months, we studied 51 patients (37 male, mean age 58.9 ± 10.0 years) with atypical chest pain or stable angina scheduled for conventional CA to determine the presence and extent of coronary artery disease. Only patients in sinus rhythm, able

to breath-hold for 20 s (which was tested before the scan), and who had never undergone angioplasty or bypass surgery, were included. Patients presenting with an acute coronary syndrome or with contraindications to iodinated contrast material (e.g., known allergy, impaired renal function, or thyroid disorders) were excluded. Our institutional review board approved the study protocol, and all patients gave written informed consent.

Patient preparation. Patients with a heart rate above 70 beats/min received a single oral dose of 100 mg metoprolol 1 h before the scan, unless contraindicated (overt heart failure or severe chronic obstructive pulmonary disease).

Scan protocol and image reconstruction. All patients were scanned on a 16-row MSCT scanner (Sensation16 Straton, Siemens, Forchheim, Germany). The scan parameters were: 16×0.75 mm collimation; rotation time 375 ms; table feed 3.0 mm/rotation; tube voltage 120 kV; effective mA: 500 to 600 (depending on age and weight/length); volumetric CT dose index 51.0 mGy, no tube modulation. A non-enhanced scan before MSCT CA was not performed. The estimated radiation exposure using this scan protocol is 11.8 to 16.3 mSv (Male-Female; WinDose, Institute of Medical Physics, Erlangen, Germany). A bolus

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Abbreviations and Acronyms

- CA = coronary angiography
- CX = circumflex coronary artery
- LAD = left anterior descending coronary artery
- LM = left main coronary artery
- MSCT = multi-slice computed tomography
- RCA = right coronary artery
- QCA = quantitative coronary angiography

of 100 ml contrast material with iodine content of 400 mg/ml (Iomeron 400, Bracco, Milan, Italy) was injected through an arm vein (rate: 4 ml/s). A bolus-tracking technique was used to synchronize the arrival of contrast in the coronary arteries and initiation of the scan. Data were acquired during a breath-hold of 18.9 ± 1.0 s.

Electrocardiographic-gated datasets were standard reconstructed during mid-to-end diastole. Generally, best image quality was obtained when reconstruction windows were positioned -350 ms before the next R-wave, or at 60% of the R-R interval. Additional reconstruction windows (e.g., early diastolic phase) were used in 29% (15 of 51) of patients. The reconstruction algorithm uses data of a single heartbeat, obtained during half a rotation time, resulting in a temporal resolution of 188 ms.

Quantitative coronary angiography (QCA). All scans were performed within two weeks before conventional CA. A single observer, unaware of the MSCT results, identified coronary segments according to the American Heart Association classification (10), and classified them as <2 and ≥ 2 mm using a QCA algorithm (CAAS, Pie Medical, Maastricht, the Netherlands). The size of the coronary arteries was determined in areas of angiographically normal appearing vessel sites, in the proximal part of the distal coronary segments and side-branches. All segments ≥ 2 mm were included for comparison with MSCT CA. Segments were classified as normal (smooth parallel or tapering borders), non-significant disease (luminal irregularities or $<50\%$ stenosis), or significant stenoses. Stenoses were evaluated in two orthogonal views, and they were classified as significant if the mean lumen diameter reduction was $\geq 50\%$.

The MSCT image evaluation. All scans were independently analyzed by two observers unaware of the results of conventional CA. All main coronary arteries and large (≥ 2 mm) side branches were evaluated irrespective of image quality. Maximum intensity projections were used to identify coronary lesions and multi-planar reconstructions to classify lesions as significant or non-significant. Disagreement between observers was resolved by consensus in a joined session. One observer re-scored all MSCT scans, and interobserver and intraobserver variability to detect significant lesions was calculated.

Statistical analysis. The diagnostic performance of MSCT CA to detect significant lesions in ≥ 2 mm coronary arteries was calculated with QCA as the standard reference and presented as sensitivity, specificity, and positive and negative predictive values with the corresponding 95% confidence intervals. Comparison between MSCT CA and QCA was performed on three levels: segment-by-segment, vessel-by-vessel (no or any disease per vessel), and patient-by-patient (no or any disease per patient). Coronary segments were scored irrespective of the score in other segments or vessels within the same patient, therefore independence among the analyses was assumed. The most proximal lesion determined the diagnostic performance in the vessel-based analysis in coronary branches with >1 stenosis.

RESULTS

Conventional CA revealed normal arteries in 16% (8 of 51), non-significant disease in 21% (11 of 51), and significant coronary artery disease in 63% (32 of 51) of patients. Nineteen patients had single-vessel disease and 13 patients had multi-vessel disease. Five patients had significant left main coronary artery (LM) disease. The mean number of included segments per patient was 12.0 ± 1.9 . All proximal and mid-coronary segments were included in the analysis. Mean heart rate during scanning was 57.1 ± 1.0 beats/min. A beta-blocker was administered before the scan in 25 of 51 patients; most (80%) were already receiving long-term beta-blockade. Interobserver and intraobserver variability

Table 1. Diagnostic Performance of Multi-Slice Computed Tomography Coronary Angiography to Detect $\geq 50\%$ Stenoses

	N	Sensitivity	Specificity	Positive PV	Negative PV
Segment-based	610	61/64 (95, 86–99)	537/546 (98, 96–99)	61/70 (87, 76–98)	537/540 (99, 98–99)
LM (1)	51	5/5 (100, 47–100)	46/46 (100, 92–100)	5/5 (100, 47–100)	46/46 (100, 92–100)
LAD (3–5)	205	24/24 (100, 85–100)	175/181 (97, 92–98)	24/30 (80, 61–96)	175/175 (100, 97–100)
CX (3–5)	172	15/17 (88, 63–99)	154/155 (99, 96–99)	15/16 (94, 69–99)	154/156 (99, 95–99)
RCA (3–4)	182	17/18 (94, 72–99)	162/164 (99, 95–99)	17/19 (90, 66–99)	162/163 (94, 96–99)
Vessel-based	202	51/53 (96, 87–99)	143/149 (96, 91–98)	51/57 (90, 78–97)	143/145 (99, 95–99)
LM	51	5/5 (100, 47–100)	46/46 (100, 92–100)	5/5 (100, 47–100)	46/46 (100, 92–100)
LAD	51	16/16 (100, 79–100)	31/35 (89, 73–96)	16/20 (80, 56–95)	31/31 (100, 88–100)
CX	50	13/14 (93, 66–99)	35/36 (97, 85–99)	13/14 (93, 66–99)	35/36 (97, 85–99)
RCA	50	17/18 (94, 72–99)	31/32 (97, 83–99)	17/18 (94, 72–99)	31/32 (97, 83–99)
Patient-based	51	31/31 (100, 88–100)	17/20 (85, 62–96)	31/34 (91, 76–97)	17/17 (100, 80–100)

Values are n, % (95% confidence interval).

CX = circumflex coronary artery; LAD = left anterior descending coronary artery; LM = left main coronary artery; PV = predictive value; RCA = right coronary artery.

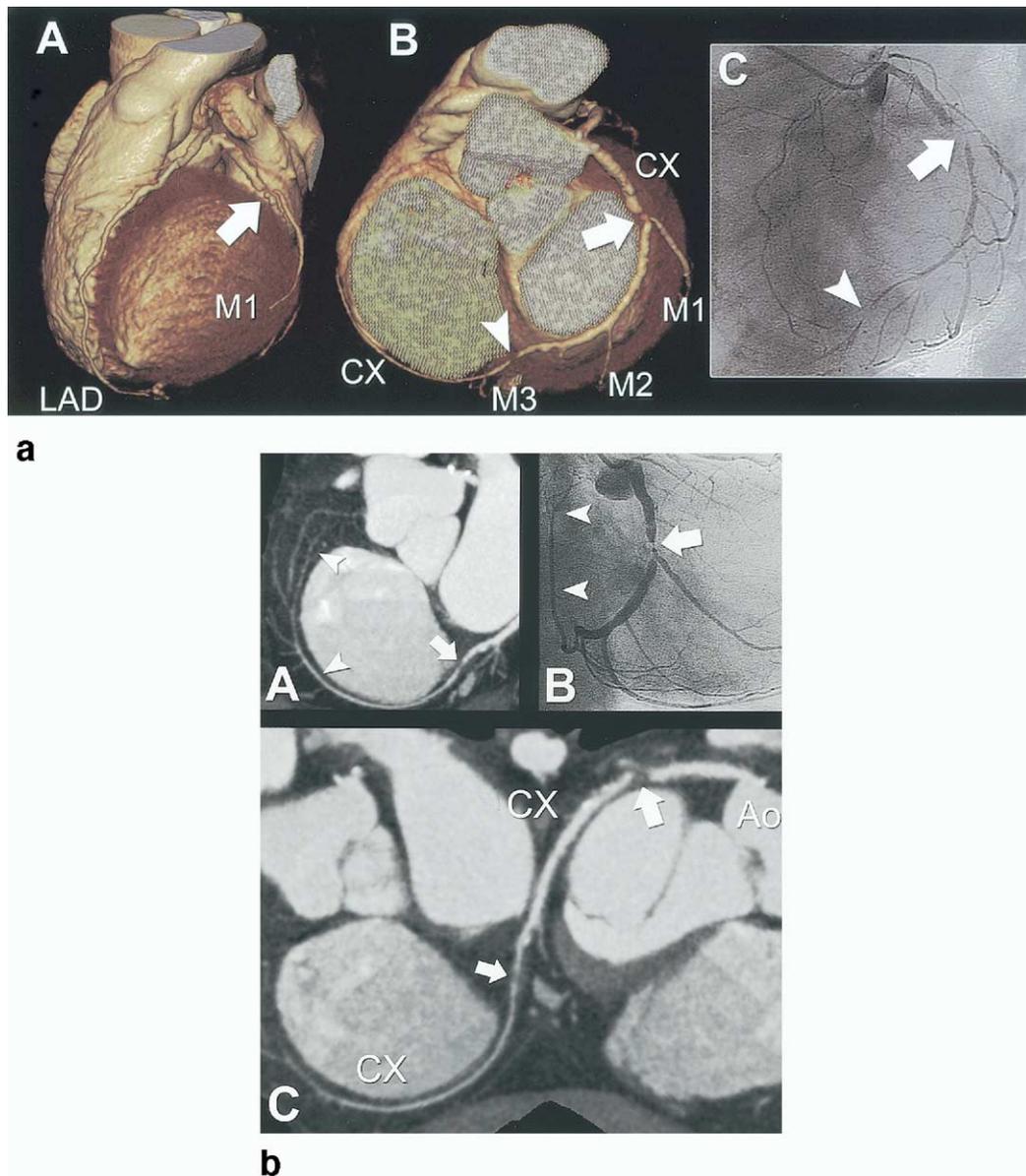


Figure 1. (a) Volume rendered computed tomography (CT) images (A, B) reveal the presence of two stenoses (arrow, arrowhead) located at the circumflex coronary artery (CX), which was confirmed on the conventional angiogram (C). (b) Maximum intensity projected (A) and curved multiplanar reconstructed (C) CT images showing the trajectory of the circumflex coronary artery (CX), which ends almost at the right coronary sinus. Arrows indicate stenoses. These findings were confirmed on conventional angiography (B). Ao = aorta; LAD = left anterior descending coronary artery; M = marginal branch.

for detection of significant lesions had kappa values of 0.73 and 0.80.

Diagnostic performance of MSCT CA. The diagnostic performance of MSCT CA to detect significant lesions is detailed in Table 1. Two significant (52% and 57% diameter reduction) lesions on QCA, located in the proximal and mid circumflex coronary artery (CX), were incorrectly classified as non-significant on MSCT. A single significant (67% diameter reduction) lesion in the distal right coronary artery (RCA) was not visualized on the MSCT scan owing to motion artifacts. No significant lesions were missed in the LM or left anterior descending coronary artery (LAD). Nine non-significant lesions on QCA were incorrectly classified as $\geq 50\%$ lesions on MSCT. On conventional CA,

four of these were non-significant lesions (mean lumen reduction 40%, range 38% to 42%), and the other five were lumen irregularities. The majority ($n = 7$) of these lesions were calcified.

On a vessel-based analysis, two significantly obstructed vessels were missed on MSCT: one RCA and one CX. Six vessels without $\geq 50\%$ lesions were incorrectly classified as significantly obstructed.

All patients with normal coronary angiograms were classified as having neither significant nor non-significant stenosis on MSCT. All patients with significant coronary artery disease were correctly identified on MSCT as having at least single-vessel disease, whereas three patients without $\geq 50\%$ lesions were classified as having single-vessel disease.

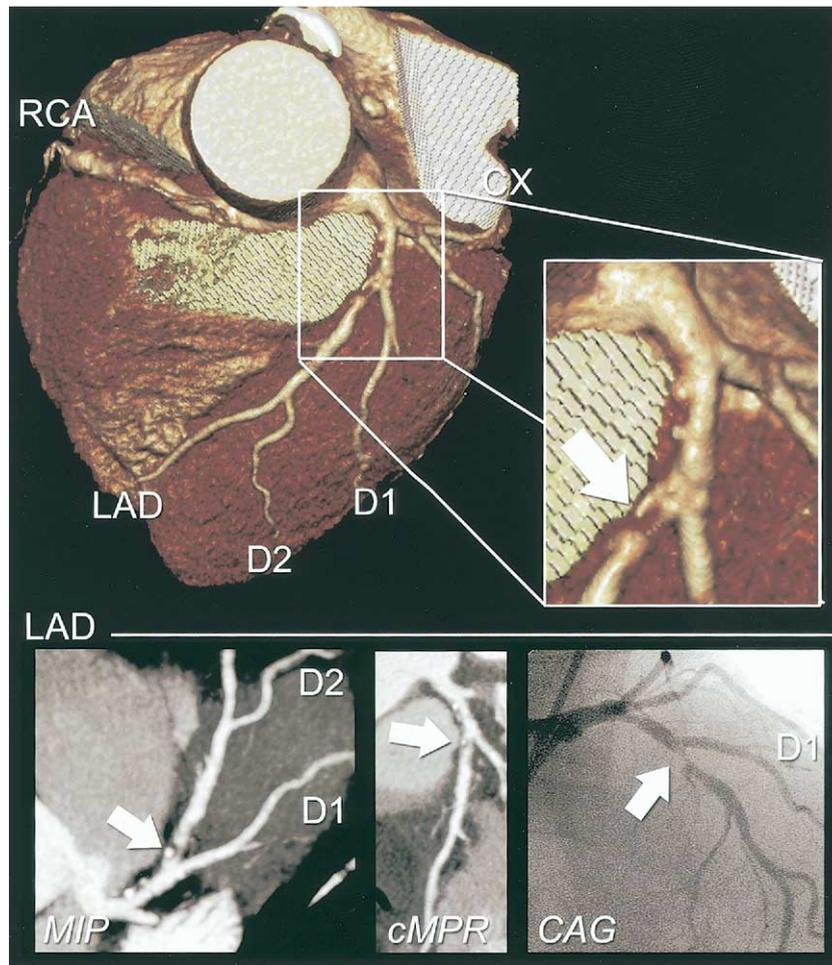


Figure 2. Volume rendered (colored image), maximum intensity projected (MIP), and curved multiplanar reconstructed (cMPR) computed tomography images demonstrate a significantly obstructed left anterior descending coronary artery (LAD) (arrow), which was confirmed on conventional angiography (CAG). CX = circumflex coronary artery; D = diagonal branch; RCA = right coronary artery.

Two examples comparing MSCT CA and conventional CA are shown in Figures 1 and 2.

DISCUSSION

Conventional CA is currently the standard technique for evaluation of patients with suspected coronary atherosclerosis. It is used both to exclude coronary atherosclerosis as a cause of symptoms and to evaluate the extent and severity of atherosclerosis with a view to referral for revascularization. Previous reports demonstrated that earlier generations of MSCT scanners showed promise for the non-invasive detection of coronary artery stenoses (1-9). Those scanners acquire fewer slices simultaneously (1-8) (4, 8, or 12 vs. 16 slices) and are equipped with a lower X-ray tube rotation speed (1-9) (500 or 420 ms vs. 375 ms) compared to the latest generation of 16-row MSCT scanners. An additional advantage of the new MSCT scanner is the ability to scan with a higher X-ray tube output, which increases the contrast-to-noise ratio and therefore image quality. These technical developments result in a markedly improved di-

agnostic performance when compared to the results reported with previous scanner generations.

Our study found that MSCT CA can detect significant stenoses with a sensitivity of 95%, a specificity of 98%, and positive and negative predictive values of 87% and 99%, respectively, when compared to conventional CA. Furthermore, all patients with normal coronary arteries on conventional CA were classified as having neither significant nor non-significant stenosis on MSCT. These results were obtained in patients with atypical chest pain or stable angina pectoris who had varying degrees of coronary artery disease ranging from no detectable significant obstructive disease to one-, two-, and three-vessel disease or LM disease.

The MSCT CA will not equal either the resolution or real-time imaging capabilities of conventional CA in the foreseeable future; however, its noninvasive nature renders the technique more patient-friendly and reduces the risk of iatrogenic injury. This technique may open new avenues for research and contribute to the development of novel management algorithms in selected patients. Potential applications include the evaluation of asymptomatic individuals at

high risk of atherosclerosis or assessment of disease progression in patients with known coronary artery disease.

Study limitations. The relatively low number of included patients was caused by limited availability of free MSCT time slots and by recruitment from a rather small local outpatient clinic. We did not investigate patients with an acute coronary syndrome, because of safety and logistic issues associated with the examination of these patients in a setting outside the coronary care unit. However, we do expect that the diagnostic performance of MSCT CA would be similar in these patients.

The limited spatial resolution of current MSCT scanners only allows qualitative assessment of coronary stenoses. Partial voluming and artifacts related to coronary calcifications seriously hamper development of reliable software able to detect and quantify the degree of coronary stenoses. However, such software would make MSCT CA a more robust and reproducible technique.

The estimated radiation dose during MSCT CA using this scan protocol is higher (11.8 to 16.3 mSv) when compared with previously reported doses using older scanner generations (6.7 to 13.0 mSv [11,12]) or conventional CA (3 to 5 mSv). Radiation exposure should be reduced by technical adjustments such as prospective X-ray tube current modulation, which limits the radiation exposure by nearly 50% in patients with low heart rates (11). However, we did not apply this feature because it limits reconstruction of images during the early-diastolic phase, which can be of importance for evaluation of the RCA.

Persistent irregular heart rhythms, such as atrial fibrillation and frequent extra-systoles, preclude MSCT CA. In some cases, motion artifacts due to an occasional extra-systole can be corrected by manual repositioning of the reconstruction windows. Severe calcification obscures the coronary lumen and can lead to overestimation of the severity of lesions due to blooming artifacts. In fact, the vast majority of false-positive lesions were calcified (7 of 9). Improvements in spatial resolution and dedicated post-processing algorithms may diminish the problem.

Motion artifacts associated with higher heart rates might be resolved by faster X-ray tube rotation time or sophisticated reconstruction algorithms that use data obtained from multiple, consecutive heartbeats.

CONCLUSIONS

The MSCT CA is a reliable technique to detect significant stenoses noninvasively in patients with stable angina and atypical chest pain. More studies are needed in other patient groups with different prevalences of disease to show that these initial favorable results are reproducible on a wider scale.

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