Effect of age and plaque morphology on diagnostic accuracy of dual source multidetector computed tomography coronary angiography

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Abstract

Background Multidetector computed tomography (MDCT) coronary angiography represents one of the most exciting technological revolutions in cardiac imaging and it has been increasingly used in the diagnosis of coronary artery disease. The purpose of this study is to investigate the effect of age and coronary plaque calcification on diagnostic accuracy of MDCT. Methods The patients were examined by using dual-source MDCT and conventional coronary angiography. MDCT results were analyzed with regard to the severity (>50% stenosis) and morphology (non-calcified, mixed, or calcified) of coronary atherosclerotic plaques evaluated in a 16-segment model. Results In total, 181 patients (94 men and 87 women) with 2,687 coronary artery segments were examined with MDCT. Ninety three patients were older than 65 years of age (group A, 42 men and 88 were younger (group B, 52 men). Two-hundred nine coronary artery segments (7.2%) were excluded because of small distal coronary vessel segments and/or motion artifacts. The overall number of segments with non-diagnostic image quality was similar in both groups of patients. Of the 2,687 evaluated segments, 157 (5.8%) were significantly diseased, and 144 of them were correctly detected by MDCT. Diagnostic evaluation showed that the sensitivity, positive predictive value, specificity, and negative predictive value were 89.5%, 62.5%, 96.0%, and 99.2%, respectively in group A, and 95.2%, 64.8%, 97.5%, and 99.8% in group B, respectively. In addition, detailed segment-based analyses in coronary segments with non-calcified, mixed and calcified plaques in both groups were similar diagnostic accuracy. Conclusions Very high diagnostic accuracy observed in this study suggests that MDCT coronary angiography could be a suitable diagnostic tool for not only younger patients but also for older patients.

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1 Introduction

The elderly represent a challenging subset of the population of patients with coronary artery disease (CAD). They are more likely to have comorbid disease, atypical presentations, and unfavorable outcomes than younger patients. The diagnosis of CAD may be more difficult with age as the symptoms of heart disease are often modified, and cardiac pain may be greatly reduced in intensity. The diagnostic evaluation and subsequent management of patients suspected of having CAD is aimed at reducing complaints and improving prognosis.⁠[1]⁠ There are several non-invasive diagnostic tools to evaluate CAD. Stress testing is useful in the diagnosis of ischemia with suspected or known coronary disease. The three most commonly used types of stress tests are the standard exercise treadmill test, stress nuclear single photon emission computed tomography, and stress echocardiography. A large proportion of the older patients may be unable to perform exercise stress tests due to the higher prevalence of pulmonary airway, degenerative joint and peripheral vascular diseases, and the reduced physical fitness of the older patients as compared to the younger.⁠[2] Conventional coronary angiography (CAG) is currently the gold standard procedure for assessment of CAD. However, CAG is invasive and associated with potentially several complications, especially with age.⁠[3] A growing number of studies have suggested that multidetector computed tomography (MDCT) is highly accurate for the exclusion of significant coronary artery stenosis (>50% luminal narrowing),
with high negative predictive values (NPV), in comparison with conventional CAG. Studies performed using 64-slice MDCT or dual-source MDCT have shown improved performance in detecting and diagnosing significant coronary stenosis in per-segment and per-patient analyses due to greater spatial and temporal resolution. At present, however, there are insufficient data on the relationship between dual source MDCT accuracy and patient age or coronary atherosclerotic plaque morphology. Therefore, we aim to determine the effect of age and plaque morphology on the diagnostic accuracy of dual source MDCT.

2 Methods

2.1 Patients and study protocol

A database of 181 patients with suspected CAD, who underwent CAG and MDCT was reviewed. Demographic information, medical history, and details of medication usage were obtained from medical records. The patients were divided into two groups (Group A or B) according to age. Group A comprised of 93 patients aged ≥ 65 years and Group B included 88 patients aged ≤ 65 years. The time interval between MDCT and CAG ranged from three days to three months depending on clinical situations, or MDCT results. Exclusion criteria were rhythm disorders other than stable sinus rhythm, intolerance to iodine contrast, renal dysfunction (serum creatinine levels ≥ 1.5 mg/dL), and pregnancy. This study was approved by the local Ethics Committee and all patients provided informed consent for the study.

2.2 MDCT coronary angiography scan

All patients underwent coronary MDCT imaging using a dual-source 64-slice MDCT scanner (Somatom Definition; Siemens, Erlangen, Germany). Sublingual nitrate (5 mg of isosorbide dinitrate, Fako Isordil) was administered 2-4 min before image acquisition to dilate the coronary arteries. The coronary angiographic scan was obtained via an injection of 80 mL of nonionic contrast medium (350 mg I/mL iomeprol, Bracco Omnipaque) at a flow rate of 6 mL/s. The contrast medium was followed by 50 mL of saline solution, at the same injection rate, to wash out the contrast material from the right ventricle. Contrast administration was controlled with bolus tracking by which a bolus of radio- opaque contrast media is injected into a patient via a peripheral intravenous cannula. Depending on the vessel being imaged, the volume of contrast is tracked using a region of interest at a certain level and then followed by the computed tomography (CT) scanner once it reaches this level. Images are acquired at a rate as fast as the contrast moving through the blood vessels. The scan parameters were detector collimation, 32 × 0.6 mm; slice acquisition, 64 × 0.6 mm; gantry rotation time, 330 ms; temporal resolution, 83 ms; pitch, 0.20–0.47 adapted to the heart rate; tube current, 390 mAs per rotation; and tube potential, 120 kVp. The scan was completed in approximately 5.7–8.4 s, depending on the cardiac dimensions and pitch, during a single breath hold and in the craniocaudal direction. Prospective electrocardiography (ECG) gating for radiation dose reduction was used for all patients. The retrospective gating technique was used to synchronize data reconstruction with the ECG signal. The reconstructions were made during all cardiac phases at 50 ms intervals at a slice thickness of 0.75 mm and a reconstruction increment of 0.5 mm. The reconstruction interval with the fewest motion artifacts was chosen and used for further analysis.

2.3 MDCT data analysis

All images were interpreted immediately after scanning by radiologists who were unaware of the clinical presentations of the patients. Coronary artery plaque (CAP) was defined as any clearly discernible structure associated with the coronary artery wall in at least two independent image planes. To better categorize the CAP, the coronary system was divided into 16 separate segments, based on a modified American Heart Association (AHA) classification, using original axial images; thin slice, maximal intensity projections; and cross-sectional reconstructions orthogonal to the long axis of each coronary segment (0.75 mm thickness). The 16 segments included the left main coronary artery; proximal, mid and distal left anterior descending arteries; proximal, mid, and distal diagonal/intermediate branches; proximal, mid and distal circumflex arteries; proximal, mid, and distal obtuse marginal branches; and proximal, mid and distal right coronary arteries. All plaque components were assessed on a per segment basis.

CAP severity was also evaluated. Non-significant CAP were defined as lesions causing ≤ 50% luminal narrowing, and significant CAP were defined as lesions causing > 50% luminal narrowing. The morphologies of the CAP were also evaluated. For each segment, CAPs were categorized as (1) none, (2) calcified plaque (CP; plaques with a CT density greater than the contrast enhanced coronary lumen), (3) non-calcified plaque (NCP; plaques with a computed tomographic density less than the contrast enhanced coronary lumen but greater than the surrounding tissue), or (4) mixed plaque (MP; plaques with both calcified and non-calcified components) (Figure 1).
3 Results

3.1 Patient characteristics

A total of 181 patients were enrolled in this study. Group A consisted of 93 (51.4%) patients older than 65 ≥ years (42 men; mean age 69.8 ± 3.8 years), and group B consisted of 88 (48.6%) patients ≤ 65 years (52 men; mean age 55.1 ± 5.8 years). According to baseline demographic characteristics, both groups were similar with regard to gender, hypertension, diabetes, dyslipidemia, smoking, family history, and body mass index. Baseline characteristics of the entire study population are shown in Table 1. More than three-fourths of the patients had atypical symptoms for CAD. Most of the remaining patients (14.4% of those enrolled) had no cardiac symptoms; MDCT had been performed for pre-operative cardiac evaluation. Excepting ten patients with known CAD, and twenty six patients with no symptoms, patients had intermediate pretest probabilities of CAD.

3.2 Lesion detection

A total of 2,687 coronary segments were analyzed for the detection of significant obstructive coronary stenosis. In group A, we evaluated 1,360 coronary artery segments. Eighty-five (89.5%) of 95 segments with significant stenosis (> 50% of lumen diameter) of the coronary vessels were correctly detected by MDCT. One thousand two hundred fourteen (96.0%) of 1,265 segments without significant stenosis were correctly classified by MDCT. In group B, we evaluated 1,327 coronary artery segments. Fifty-nine (95.2%)

Table 1. Baseline characteristics of the study population.

|                      | All Patients (n = 181) | Group A (n = 93) | Group B (n = 88) | P value |
|----------------------|------------------------|------------------|------------------|---------|
| Age                  | 62.66 ± 8.9            | 69.8 ± 3.8       | 55.1 ± 5.8       | < 0.001 |
| Male gender          | 94 (51.9)              | 42 (45.2)        | 52 (59.1)        | 0.061   |
| Hypertension         | 135 (74.6)             | 74 (79.6)        | 61 (69.3)        | 0.113   |
| Diabetes             | 45 (24.9)              | 22 (23.7)        | 23 (26.1)        | 0.700   |
| Dyslipidemia         | 246 (77.6)             | 68 (73.1)        | 68 (77.3)        | 0.518   |
| Smoking              | 75 (41.4)              | 33 (35.5)        | 42 (47.7)        | 0.095   |
| Family history of premature CAD | 18 (9.9)              | 5 (5.7)          | 13 (14.0)        | 0.062   |
| Body mass index, kg/m² | 28.2 ± 3.9            | 27.7 ± 4.5       | 28.7 ± 3.9       | 0.389   |
| Symptoms             |                        |                  |                  |         |
| Asymptomatic         | 26 (14.4)              | 15 (16.1)        | 11 (12.5)        | 0.433   |
| Atypical angina      | 77 (42.5)              | 41 (44.1)        | 36 (40.9)        | 0.569   |
| Non-cardiac pain     | 71 (39.2)              | 36 (38.7)        | 35 (39.8)        | 0.906   |
| Typical angina       | 7 (3.9)                | 1 (1.1)          | 6 (6.8)          | 0.060   |

Data are presented as mean ± SD or n (%). Group A: > 65 years old, Group B: < 65 years old. CAD: coronary artery disease.
of 62 segments with significant stenosis of the coronary vessels were correctly detected by MDCT. One thousand two hundred thirty-three (97.5%) of 1,265 segments without significant stenosis were correctly classified by MDCT. Additionally, diagnostic analyses were performed on a per-artery basis and per-patient basis. The diagnostic performance of MDCT in detecting significant lesions on a per-segment, per-vessel, and per-patient basis is detailed in Table 2. Image quality was assessed semi-quantitatively and some coronary segments were excluded from the analysis in the presence of poor image quality. Two hundred and nine coronary artery segments (7.2%) were excluded because of small coronary vessel diameter \((n = 98, 3.4\%)\), extensive vessel wall calcification \((n = 79, 2.7\%)\), and motion artifacts \((n = 32, 1.1\%)\). There was not statistically significant difference about the overall number of segments with non-diagnostic image quality in both groups of patients.

### 3.3 Coronary artery plaque morphology

Of the 2,687 coronary segments, 1,814 (67.5% of 2,687) coronary segments did not have any type of CAPs, while the remaining 873 segments had CAP. Of those with CAP, 613 (70.2% of 873) segments were classified as NCP, 146 (16.7%) as MP, and 114 (13.1%) as CP. Older patients showed a significantly higher ratio of MP and CP compared with younger patients (15.3% vs. 10.3%, and 20.2% vs. 12.6%, respectively; \(P < 0.001\)). Conversely, the level of NCP was lower in older patients than in younger patients (64.5% vs. 77.1%; \(P = 0.968\)) but this did not reach statistical significance. CAP characteristics in both groups are shown in Table 3. The diagnostic analysis of coronary segments containing CP demonstrated that sensitivity, specificity, positive predictive value (PPV), and NPV of MDCT compared with CAG were 81.8, 97.1, 75.0, and 98.0, respectively. Detailed segment-based analyses of NCP, MP and CP in all patients are shown in Table 4. These results revealed that there were high diagnostic accuracy of MDCT in coronary segments with NCP, MP and CP (Figure 2).

### Table 2. Segment, vessel and patient-based diagnostic accuracy of dual-source MDCT in study patients.

| Segment-based | LAD | CX | RCA |
|---------------|-----|----|-----|
| Group A       | Group B | Average | Group A | Group B | Average | Group A | Group B | Average |
| Sensitivity   | 89.5 | 95.2 | 91.7 | 93.5 | 100 | 95.7 | 86.7 | 84.6 | 85.7 |
| PPV           | 62.5 | 64.8 | 63.4 | 74.4 | 64.0 | 70.3 | 48.1 | 78.6 | 58.5 |
| Specificity   | 96.0 | 97.5 | 96.7 | 83.9 | 87.5 | 85.8 | 81.8 | 96.0 | 88.8 |
| NPV           | 99.2 | 99.8 | 99.5 | 96.3 | 100 | 98.3 | 96.9 | 97.3 | 97.1 |

Group A: > 65 years old; Group B: < 65 years old. CX: circumflex artery; LAD: Left anterior descending artery; MDCT: Multidetector computed tomography; NCP: Negative predictive value; PPV: Positive predictive value; RCA: Right coronary artery.

### Table 3. Coronary artery plaque morphology.

| Plaques       | Group A | Group B | \(P \) value |
|---------------|---------|---------|--------------|
| Segments      | %       | %       |              |
| Non-calculated| 307     | 306     | 0.968        |
| Mixed         | 96      | 50      | 12.6         | < 0.001    |
| Calcified     | 73      | 41      | 10.3         | 0.003      |

Group A: > 65 years old; Group B: < 65 years old.

### Table 4. Diagnostic analysis of MDCT according to plaque morphology in both groups.

| Segments with non-calculated plaques | Segments with mixed plaques | Segments with calcified plaques |
|--------------------------------------|----------------------------|--------------------------------|
| Group A | Group B | Average | Group A | Group B | Average | Group A | Group B | Average  |
| Sensitivity | 84.8 | 90.0 | 86.8 | 99.0 | 77.8 | 88.9 | 90.0 | 66.7 | 81.8 |
| PPV | 52.8 | 58.1 | 54.8 | 75.0 | 99.0 | 84.2 | 90.0 | 66.8 | 75.0 |
| Specificity | 90.9 | 95.5 | 93.2 | 96.6 | 99.0 | 97.7 | 98.4 | 97.0 | 97.1 |
| NPV | 98.0 | 99.3 | 98.7 | 99.0 | 95.3 | 98.4 | 98.4 | 97.0 | 98.0 |

Group A: > 65 years old; Group B: < 65 years old. MDCT: multidetector computed tomography; NPV: negative predictive value; PPV: positive predictive value.
have been used to detect CAD, such as exercise testing or pharmacologic cardiac imaging (nuclear or echocardiography), which can only detect high-grade coronary stenosis. As we know, the severity of narrowing observed in coronary angiographic images is a poor predictor of subsequent acute myocardial infarction, and about 60% to 83% of heart attacks occur at the site of a non-obstructive plaque.\textsuperscript{[19]} These diagnostic tools cannot identify a vast number of asymptomatic at-risk patients. The prognostic role of MDCT-detected CAP morphology—specifically, the ability of MDCT to detect non-critical CAP morphology—has also been evaluated in several studies.\textsuperscript{[20]} Among patients with suspected CAD, Russo, et al.\textsuperscript{[21]} found that the major cardiac event rate was significantly higher in patients with MP and/or NCP CAPs, as compared to patients with CP. In a prognostic study, Carrigan, et al.\textsuperscript{[22]} showed that patients with no CAPs revealed by MDCT had a 100% event-free survival rate over a follow-up period of 2.3 years.

It is not surprising that the detection and treatment of CAD may involve a somewhat different set of considerations for older patients compared to younger. Prior to this study, no data existed in the literature on the correlation between the accuracy of dual source MDCT and the patient’s age. The present study showed that MDCT had similar diagnostic accuracy for older and younger patients. Although sensitivity and positive predictive values were slightly lower for older patients compared to younger (89.5% and 62.5%, vs. 95.2% and 64.8%, respectively), specificity and negative predictive values were similar for both groups (96.0% and 99.2%, vs. 97.5% and 99.8%, respectively). Arrhythmia, motion artifacts, and breathing during scans caused a decline in diagnostic accuracy. Dual-source MDCT includes some improvements which overcome these problems and result in high-quality, nearly motion-free images. Apart from heart rate and respiration, coronary calcifications may influence image quality, and older patients are more likely to have calcification of the coronary tree.\textsuperscript{[23]} On MDCT images, large and dense CP cause blooming artifacts and result in a virtual increase in plaque volume, thus, potentially obscuring the coronary lumen.\textsuperscript{[24]} In our study, we found a slight deterioration in the sensitivity and PPV when completing per-segment analysis but a negligible decrease in the specificity and negative predictive value. Contrastingly, we found a significant decrease in specificity during per-patient analysis but a milder decrease in the NPV. This reduction in specificity can be explained statistically. Specificity is likely to be lower at the patient level, compared to the segmental level, because on a per-patient basis, many segments have the potential to provide false-positives. The likelihood of a false-positive oc-
occurring among all of a patient’s segments is higher than the likelihood of a false-positive occurring in a single segment, hence the lower patient specificity.

Previous studies of the influence of calcification on the diagnostic accuracy of MDCT provide scientific data which is somewhat difficult to apply to clinical practice. As we expected, the number of MP and CP were higher in older patients than in younger patients [older patients: 96 MP (20.2%) and 73 CP (15.3%), respectively; younger patients: 50 MP (12.6%) and 41 CP (10.3%), respectively]. Besides diagnostic analysis, the most important finding of the present study is that age actually increased calcification in the CAP, which did not severely affect the diagnostic accuracy of noninvasive MDCT imaging, especially in terms of the specificity and NPV (older patients: 96.0% and 99.2%, respectively; younger patients: 97.5% and 99.8%, respectively). Our findings indicate that MDCT is an acceptable diagnostic tool, not only for younger, but also for the older individuals.

As a small, single-center study, our study has some limitations. Firstly, some part of the coronary segments had to be removed from the diagnostic accuracy analysis. Nevertheless, majority of these segments were distal small part of coronary arteries. We thought that exclusion of these segments did not significantly affect the diagnostic results. Secondly, patients with CAD (stent implantation or bypass surgery) were not enrolled in the present study; therefore, further research is needed to evaluate the degree of accuracy in these older patients. Although plaque morphology was specified as NCP, MP, or CP, the calcium score was not evaluated. Finally, our study selection criteria may have introduced a bias as only patients with intermediate pre-test probabilities of CAD who were referred to our hospital were included in the study.

In conclusion, dual-source MDCT is highly accurate in diagnosing, or excluding, significant coronary stenosis as compared with the standard reference conventional CAG. Although age and coronary calcification have an impact on MDCT image quality, diagnostic accuracy is high to warrant consideration of MDCT as a diagnostic tool even in older patients.

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