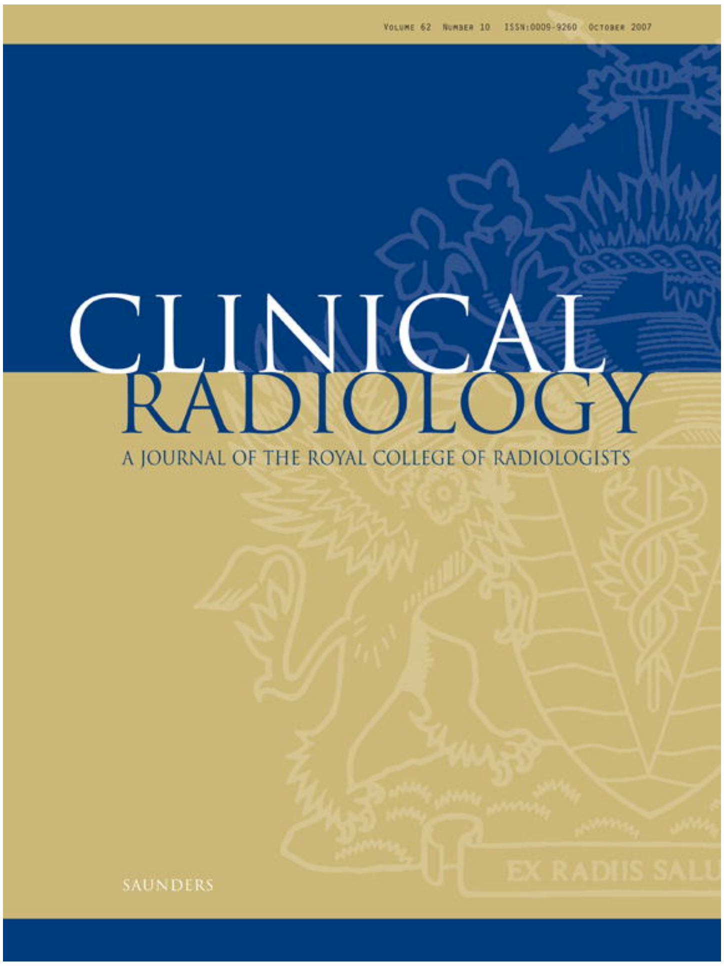
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Accuracy of multidetector spiral computed tomography in detecting significant coronary stenosis in patient populations with differing pre-test probabilities of disease

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AIM: To investigate the clinical impact of multidetector computed tomography (MDCT) in patients with a low versus a high pre-test likelihood of coronary artery disease (CAD).

MATERIALS AND METHODS: A cohort of 120 patients with suspected CAD, scheduled for conventional coronary angiography, underwent MDCT. Using the American Heart Association (AHA)/American College of Cardiology (ACC) guidelines, the population was divided into two groups: patients with a low (group 1) and a high (group 2) likelihood of CAD.

RESULTS: Analysis of all segments showed a high feasibility (92%), and a patient based-model showed excellent sensitivity and negative predictive values (NPV; both 100%) and acceptable specificity and positive predictive values (PPV; 86 and 90%, respectively), with an accuracy of 94%. Using MDCT in patients with lower pre-test likelihoods of CAD, according to the ACC/AHA guidelines, the accuracy remained high (93%); conversely, in patient groups with a high prevalence of CAD, a non-significant reduction in accuracy (85%) occurred using MDCT. Particularly, MDCT can be used effectively to exclude a diagnosis of CAD because of its high sensitivity and NPV (100%), but shows a significant reduction in specificity (58%). This reduction was due to an increase in the false-positive:true-negative ratio because of the higher percentage of calcified plaque (a relative but non-significant increase in false positives), and the high prevalence of CAD (significant reduction in true negatives). No differences were found between MDCT and quantitative coronary angiography (QCA) concerning the number of vessels narrowed.

CONCLUSION: Because of its excellent sensitivity and specificity in patients with a low pre-test likelihood of CAD, MDCT could be helpful in clinical decision-making in this population.

Introduction

Multidetector computed tomography (MDCT) has recently been introduced as a promising method for non-invasive imaging of epicardial coronary artery disease (CAD). Previous studies have shown high feasibility and sensitivity, good specificity associated with negative (NPV) and positive predictive values (PPV) of 95–98% and 80%, respectively.[1–12] However the accuracy of MDCT in detecting significant coronary stenosis in patients with different pre-test likelihoods of disease has been evaluated in few studies. In this regard, Hoffman et al.[13] proposed a patient-based model showing that MDCT has moderate diagnostic value for the exclusion of significant obstructive coronary stenosis in a population with a high prevalence of CAD (NPV 75%). Conversely, Nikolaou et al.[14] showed that MDCT had a high NPV (99%) in patients with a low pre-test likelihood of significant disease. So far, few data are available concerning the accuracy of MDCT in patients with different pre-test likelihoods of CAD.[15] The aim of this study was to test the accuracy of MDCT in detecting a significant coronary stenosis as compared with invasive coronary angiography in populations with low and high pre-test likelihood of CAD.

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Materials and methods

Study population

Over a period of 8 months, 120 consecutive patients (82 men, age 62 ± 10 years) with a history of chest pain, scheduled for conventional coronary angiography, were studied. Exclusion criteria were contraindications to the administration of iodinated contrast media, history of coronary revascularization (previous bypass graft surgery or coronary stent implantation), renal insufficiency (serum creatinine >2 mg/dl), and possible pregnancy. Other technical contraindications were: presence of cardiac pacemakers, inability to sustain a breath-hold for 25 s, body mass index >40, atrial fibrillation or flutter, heart rate >75 beats/min despite β-blockade treatment.

At admission the pre-test likelihood of CAD was defined using an estimated predicted probability according to American Heart Association (AHA)/ACC guidelines for the management of chronic stable angina, based on age, sex, and symptoms.[16] Two types of chest pain were considered: atypical angina including atypical location of chest pain; very prolonged and repeated pain unrelated to exercise and not relieved by rest or nitro-glycerine; and typical angina defined as substernal chest pain that is exertional in nature and relieved promptly by nitro-glycerine therapy. On the basis of these criteria two groups were defined: patients with a low (group 1) and patients with a high (group 2) pre-test likelihood of CAD.

Study protocol

All patients underwent MDCT and conventional coronary angiography (the mean ± SD interval between these tests was 19 ± 11 days). All patients gave written informed consent, and the institutional ethical committee approved the study protocol.

MDCT protocol

Metoprolol was administered intravenously before MDCT with a titration dose up to 15 mg if the heart rate was >75 beats/min (mean dose plus standard deviation: 4.8 ± 1.2 mg). MDCT data were acquired using a 16-section CT machine (GE Medical Systems Light Speed Pro, Waukesha, WI, USA). A calcium score examination was performed with the following parameters: individual detector width 2.5 mm, gantry rotation time 400 ms, tube voltage 120 kV, tube current 150 mA. The MDCT parameters for evaluation of coronary arteries were: individual detector width 0.625 mm, gantry rotation time 400 ms, tube voltage 120 kV; in accordance with the ''electrocardiogram (ECG)-pulsing technique'' the tube current was modulated with a maximum current of 600 mA during a period between 40–80% of the R-wave to R-wave interval and a reduction by 80% during the remaining cardiac cycle leading to an estimated mean effective radiation dose of approximately 12 mSv.

During the examination, a variable dose of contrast agent (Iomeron 400 mg/ml Bracco, Milan, Italy, mean dose 110 ml ± 11 ml) was injected intravenously at a rate of 4.5 ml/s. To reduce the contrast agent volume[17] and hyper-attenuation in the superior vena cava and right heart,[18] a saline solution (30 ml at 2 ml/s) was injected immediately after the contrast agent bolus. MDCT images were acquired by the fluoroscopic bolus tracking technique (as soon as the signal density level in the ascending aorta reached a predefined threshold of 100 HU, acquisition of the CT data was started) during breath-hold (generally about 20 s).

The MDCT datasets were analysed by three expert readers using volume rendering (VR), multiplanar reconstruction (MPR) and vessels analysis (VA) software packages (CardioQ3 package GE Medical Systems) for each patient. Disagreements were resolved by consensus.

MDCT image evaluation

The coronary calcium score was assessed with a dedicated software application (CaScore, GE Medical Systems); the overall Agatston score[19] was recorded for each patient. The coronary arteries were classified according to the 16-segment model of the AHA.[20] The grading criteria for image quality were based on the presence of calcified plaque that precluded the assessment of the coronary lumen, motion artefacts, misalignment of sections related to irregular heart beats, and image noise/suboptimal contrast enhancement. According to these criteria, the image quality of all vessels was classified as good, adequate, or poor. The segments with a diameter ≤1.5 mm at quantitative analysis were excluded from the analysis, whereas segments classified as having poor image quality were defined as not assessable.

Any narrowing of the normal contrast-enhanced lumen by≥50% that could be identified in at least two independent planes was defined as significant coronary artery stenosis; on the basis of the presence and number of stenoses each patient was classified as healthy or affected by one, two, or three-vessel disease. Disagreements were resolved by consensus.

Table 1 Baseline characteristics of the study population

	All population	Group 1	Group 2
Number and percentage of patients	116 (100%)	69 (59%)	47 (41%)
Age (years)	62 ± 10	60 ± 10	66 ± 9*
Sex (male/female)	82/34	50/19	40/7
Heart rate (beats/min)	61 ± 9	62 ± 9	61 ± 9
Normal coronary artery [*n* (%)]	50 (43%)	41 (59%)	12 (25%)*
Coronary artery disease [*n* (%)]	66 (57%)	28 (41%)	35 (75%)*
One vessel [*n* (%)]	25 (21%)	10 (14%)	13 (28%)
Two vessel [*n* (%)]	27 (23%)	14 (20%)	11 (23%)
Three vessel [*n* (%)]	14 (12%)	4 (6%)	11 (23%)

*$p < 0.05$ Group 2 vs Group 1.

Selective coronary angiography

Selective coronary angiography was performed with standard techniques through a transfemoral approach. The coronary arteries were divided into segments according to the AHA classification.[20] The angiograms were assessed with quantitative coronary angiography software (QCA; CAAS, Pie Medical, Maastricht, Netherlands) by an independent interventional cardiologist blinded to clinical and MDCT data. The severity of coronary stenosis was quantified on two orthogonal views, and a stenosis was classified as significant if the mean lumen diameter reduction was ≥50%.

Statistical analysis

The Agatston score[19] was recorded for each patient and differences between groups were measured using the Mann–Whitney test for unpaired data. The feasibility of the MDCT image was measured as number of assessable vessels versus total number of vessels. Estimations of the sensitivity, specificity, negative predictive value (NPV), positive predictive value (PPV), and accuracy were calculated on a vessel model and on a patient model (these diagnostic parameters are expressed with a 95% confidence interval). Differences between groups were tested by the Student's *t*-test for unpaired data and the accuracy of the MDCT examination was tested in these groups, differences being analysed by the chi-squared test.

Results

Clinical characteristics of the study population are listed in Table 1. According to the ACC/AHA guidelines, 69 patients (59%) belonged to group 1, and 47 patients (41%) belonged to group 2. Thirty-one percent of the patients (37 out of 120) received an intravenous beta-blocker (metoprolol: mean dose 4.8 ± 1.2 mg) immediately before the procedure. The mean heart rate of the study population was 61 ± 9 beats/min during the procedure. Four patients with a heart rate >75 beats/min were excluded from the study. The mean breath-hold duration was 20 ± 2 s. MDCT was performed without complications in all cases.

Based on invasive coronary angiography, the prevalence of CAD was 57% (66 out of 116 patients; 25 with one-vessel disease; 27 with two-vessel disease; 14 with three-vessel disease). No differences were found in terms of heart rate between group 1 and group 2. Group 1 patients were slightly younger than group 2 patients, and the prevalence of CAD in this group was lower (41%) than in group 2 (75%; $p < 0.005$).

Vessel-based analysis

Table 2 lists the feasibility and accuracy of MDCT in the study population. The feasibility of the

Table 2 Feasibility and accuracy of evaluation of coronary vessels by multidetector computed tomography versus quantitative coronary angiography in a vessel model based on AHA-segment classification

Vessels	Feasibility	Sensitivity	Specificity	PPV	NPV
LM	99%	100%	96%	50%	100%
LAD	96%	97%	92%	94%	96%
D1	96%	83%	94%	71%	97%
D2	82%	100%	100%	100%	100%
LCX	91%	100%	94%	88%	100%
M1	92%	75%	88%	43%	97%
M2	64%		100%		100%
RCA	92%	100%	83%	79%	100%
PDA	87%	60%	100%	100%	96%
PLA	95%	100%	97%	82%	100%
All Vessels	92%	100% (95% CI: 100–100%)	86% (95% CI: 82–88%)	91% (95% CI: 86–93%)	100% (95% CI: 100–100%)

LM, left main artery; LAD, left anterior descending artery; D1, first diagonal branch; D2, second diagonal branch; LCX, left circumflex artery; M1, first diagonal branch; M2, second marginal branch; RCA, right coronary artery; PDA, posterior descending artery; PLA, posterior-lateral artery; PPV, positive predictive value; NPV, negative predictive value; 95% CI, 95% confidence interval.

technique was 92% for all vessels (1067 out of 1160 vessels). Overall the NPV was very high, whereas the PPV was variable depending on the vessel examined (from 50% for the left main artery to 100% for the posterior descending artery). Particularly, the low PPV of the left main artery was due to the low prevalence of disease in this segment (true positive) and was not related to a higher number of false positives, which were similar to other vessels.

Patient-based analysis

Table 3 lists the Agatston calcium score, the sensitivity, specificity, NPV, PPV, and accuracy of MDCT in a patient-model analysis. Group 2 patients had a significantly higher calcium score ($p < 0.01$). Forty-three out of 50 patients without significant CAD were correctly identified by MDCT and the remaining seven patients were incorrectly classified as having at least one-vessel disease; MDCT correctly identified 66 out of 66 patients with CAD (100%) without any false negatives.

The sensitivity for classification of patients with and without coronary stenosis (narrowing > 50%) was 100%, the specificity was 86%, the NPV was 100%, the PPV was 91%, and the accuracy was 94% (all results are expressed with 95% confidence interval).

Figs. 1 and 2 show examples of MDCT performed in two patients of group 1. MDCT in the first case (Fig. 1) excluded coronary artery lesions, whereas Fig. 2 shows an example of a significant and isolated narrowing of the left anterior descending artery confirmed by coronary angiography in a case of atypical angina and one single episode of syncope at effort in a patient in whom all non-invasive tests were negative.

Table 3 also shows the accuracy of the technique in groups 1 and 2. In group 1 the sensitivity, specificity, NPV, PPV and accuracy were 100, 88, 100, 85, and 93%, respectively; in group 2 despite a non-significant reduction of accuracy (89%), the specificity was significantly lower (58%) than in group 1. In group 1, three out of five false positives were due to overestimation of calcified plaque, one false positive was due to an artefact secondary to misalignment of sections, and one was due to overestimation of fibrotic plaque. In group 2, all five false-positive cases were due to blooming effects of calcified plaque.

The results indicate that MDCT overestimates CAD, but no significant differences were found in terms of number of vessels narrowed (Table 4).

Table 3 Feasibility and accuracy of evaluation of coronary vessels by multidetector computed tomography versus quantitative coronary angiography in a vessel model based on AHA-segment classification

Patients	Number	TP	TN	FP	FN	Sensitivity	Specificity	NPV	PPV	Accuracy
All population	116	66	43	7	0	100% (CI:100–100%)	86% (CI:76–96%)	100% (CI:100–100%)	90% (CI:84–97%)	94% (CI:90–98%)
Agatstone score	197 ± 176									
No CAD/CAD	50/66									
Group 1	69	28	36	5	0	100% (CI:100–100%)	88% (CI:78–98%)	100% (CI:100–100%)	85% (CI:73–97%)	93% (CI:87–99%)
Agatstone score	152 ± 147									
No CAD/CAD	41/28									
Group 2	47	35[a]	7[a]	5	0	100% (CI:30–86%)	58%[b] (CI:100–100%)	100% (CI:100–100%)	87% (CI:77–98%)	89% (CI:81–98%)
Agatstone score	261 ± 196[a]									
No CAD/CAD	12/35									

CAD, coronary artery disease; TP, true positive; TN, true negative; FP, false positive; FN, false negative; NPV negative predictive value; PPV, positive predictive value; CI, 95% confidence interval.

[a] $p < 0.01$ Group 2 versus group 1.

[b] $p < 0.05$ Group 2 versus group 1.

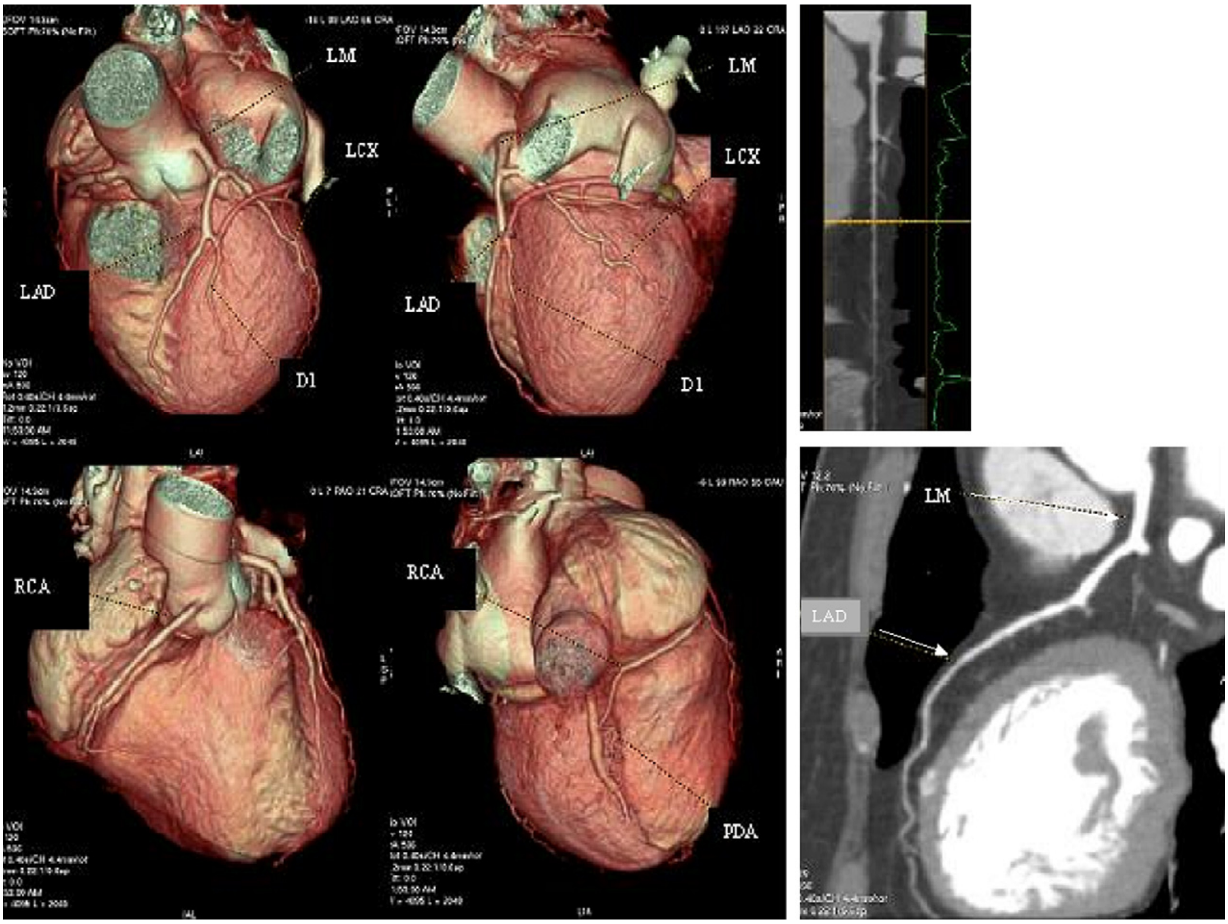

Figure 1 A patient with a positive stress test, but normal coronary vessels. Volume rendering (VR) reconstruction (left panel), vessel analysis (VA), and multiplanar reconstruction (MPR) (right panel) of coronary artery. LM, left main; LAD, left anterior descending artery; D1, first diagonal branch; LCX, left circumflex artery; RCA, right coronary artery; PDA, posterior descending artery.

Discussion

The most important findings of the present study are that MDCT provides different results for non-invasive detection of suspected CAD patients depending on the pre-test likelihood of CAD (according to ACC/AHA guidelines), and that patient groups with a low prevalence of CAD can benefit more from an MDCT examination of the coronary arteries.

MDCT has recently emerged above other competing technologies as a practical alternative to invasive coronary angiography.[21] However, the majority of previous studies evaluated the accuracy and clinical value of the technique in selected populations with known or suspected coronary artery disease, although few studies have evaluated a clinically more useful patient-based model applied to populations with a different pre-test likelihoods of CAD. In clinical practice MDCT may potentially be more useful in the diagnostic work-up of patients with a low pre-test likelihood of CAD in which the evaluation of the coronary arteries is mandatory. This is an important segment of the population undergoing standard coronary angiography, which contributes to the high percentage of invasive studies that produce normal results — procedures that could potentially be avoided by MDCT. In the present study, 120 consecutive patients without previous history of CAD, scheduled for coronary angiography, were studied. The pre-test likelihood of CAD defining group 1 (patients with low likelihood of CAD) and group 2 (patients with high likelihood of CAD) was estimated: the results not only confirmed the high accuracy of MDCT in excluding coronary lesions from the diagnosis, but also clearly demonstrated that this technique was more useful in groups with a lower prevalence of CAD. In this subgroup of patients MDCT had a high NPV (100%) and a good PPV (85%); conversely, in groups with a high prevalence of CAD the results showed a high sensitivity and NPV (100%), associated with a significant lower specificity (58%).

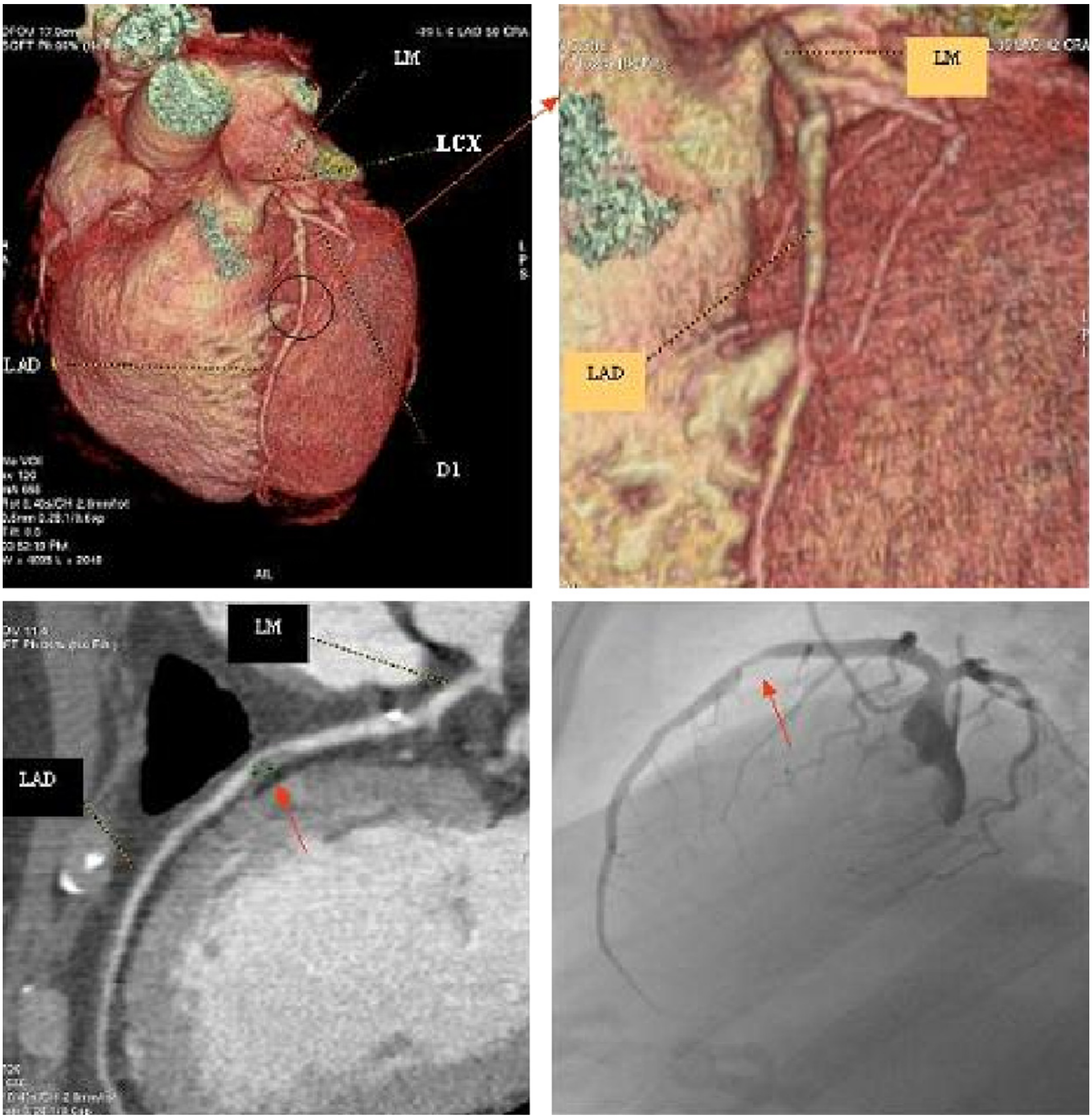

Figure 2 A patient with a history of syncope during effort, but having negative non-invasive tests. MDCT showed a significant and isolated narrowing of the left anterior descending artery (upper panel) confirmed by coronary angiography (lower panel). LM, left main artery; D1, first diagonal branch.

Hoffman et al.[13] demonstrated that MDCT provides high accuracy for non-invasive detection of suspected CAD. In their population the majority of cases (98%) had an intermediate or high probability of CAD, and if MDCT had been used as an initial diagnostic test more than 40% of patients could have avoided unnecessary invasive coronary angiography. The present results show that MDCT has a high accuracy in excluding significant CAD independently of cardiovascular risk, but in the population with a high prevalence of CAD (using selection criteria of patients with typical angina), MDCT produces a significant number of false positives despite a low number of true-negative cases (low specificity), potentially leading to an increase of unnecessary coronary angiography. The high Agatston Score in patient groups with a high prevalence of CAD may explain the increased false-positive:true-negative ratio as the blooming effect due to calcified plaque is the most important cause of false-positive cases in the present population.

These findings are in agreement with previous studies[1–12] and suggest that MDCT may be used as a more appropriate test in a population with a low

Table 4 Accuracy of detecting the number of vessels narrowed of multidetector computed tomography (MDCT) versus quantitative coronary angiography (QCA) in a patient-based model

	No CAD	CAD	One vessel	Two vessel	Three vessel
All population					
MDCT	43	73	25	29	19
QCA	50	66	25	27	14
Group 1					
MDCT	36	33	9	16	8
QCA	41	28	9	15	4
Group 2					
MDCT	7	40	17	12	11
QCA	12	35	14	12	9

MDCT: multidetector computed tomography; QCA: quantitative coronary angiography; CAD: coronary artery disease.

pre-test likelihood of CAD. In these patients MDCT, with its high NPV and good specificity, may be a conclusive test, particularly in the presence of atypical characteristics of chest pain and clinical features (age, sex) indicative of a low pre-test likelihood of CAD.

The main radiation dose was approximately 12 mSv due to the electrocardiogram (ECG)-pulsing technique that reduces total radiation dose by about 60%. Obviously adequate patient selection will be critically important and the present results do not define the role of MDCT on the basis of other diagnostic and prognostic information derived from cardiovascular risk factors and stress tests. This study also confirms the high feasibility (92%) and accuracy of MDCT in the evaluation of the majority of coronary segments including all main coronary branches. The feasibility and accuracy of the technique were, in fact, significantly lower in comparison with other segments only in small vessels, and in particular, when evaluating the second diagonal, marginal braches and posterior descending coronary arteries. This observation is in agreement with previous studies. Even though this may represent a limitation of the technique, small vessel diseases are not generally treated by revascularization and therefore the clinical role of MDCT is not significantly affected by these findings.

A major limitation of the present study is that the results were obtained using a 16-section CT machine. In fact, several reports[10–12] have demonstrated 64-section CT to be more robust and to provide better results than 16-section CT. Nevertheless, Leschka et al.[10] reported that calcium deposits were found to be responsible for all false-positive cases and Raff et al.[11] showed extreme calcification reduced specificity by up to 67%. Thus the improvement of spatial and temporal resolution of 64-section CT can lead to a reduction in false-positive cases in the group with a low pre-test likelihood of CAD because of a low calcium score, whereas such changes may not be observed in patients with a high pre-test likelihood of CAD.

In conclusion, MDCT enables the reliable detection of significant coronary lesions in a population with a low or high pre-test likelihood of CAD. However, in patient groups with a low prevalence of CAD the very high sensitivity and negative predictive value suggest an important clinical role of MDCT, particularly in cases where the purpose is to exclude CAD, thereby avoiding unnecessary invasive procedures. Conversely, in patients with a high pre-test likelihood of CAD, MDCT shows a lower specificity, despite its excellent negative predictive value, suggesting stress test or conventional coronary angiography as the ideal methods to evaluate patients with typical angina. The focus of future studies should be to determine in what clinical setting CT coronary angiography is of most value for early detection of CAD, and how MDCT can compete with other non-invasive diagnostic tests.

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