

Diagnostic work-up of unselected patients with suspected coronary artery disease: complementary role of multidetector computed tomography, symptoms and electrocardiogram stress test

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Aim We evaluated the accuracy of multidetector computed tomography in detecting coronary artery disease and how it could change the indication to coronary angiography in patients with suspected cardiac chest pain.

Methods and results We enrolled 142 consecutive patients who had already performed an exercise electrocardiogram test referred to our hospital and scheduled for coronary angiography for chest pain. According to the characteristics of chest pain and the results of exercise electrocardiogram, patients were divided into four groups: atypical chest pain and negative exercise electrocardiogram (group 1); typical chest pain and negative exercise electrocardiogram (group 2); atypical chest pain and positive exercise electrocardiogram (group 3); and typical chest pain with positive exercise electrocardiogram (group 4). We evaluated the accuracy of multidetector computed tomography and whether it could reduce the number of unnecessary coronary angiography in the study groups. Of 1801 segments larger than 1.5 mm, 1696 (94%) were assessable. In a segment based-model, sensitivity, specificity, negative predictive value, positive predictive value and accuracy were 81% (95% confidence interval 75–89%), 94% (95% confidence interval 90–98%), 96% (95% confidence interval 93–98%), 75% (95% confidence interval 69–82%) and 91% (95% confidence interval 89–93%), respectively. In a patient-based model, sensitivity, specificity, negative predictive value, positive predictive value and accuracy were 95% (95% confidence interval 91–99%), 78% (95% confidence interval 67–89%),

88% (95% confidence interval 79–97%), 89% (95% confidence interval 83–95%) and 89% (95% confidence interval 84–94%). Unnecessary coronary angiography may be avoided by multidetector computed tomography results particularly in group 2 (16%) and group 3 (24%), whereas in groups 1 and 4 the role of multidetector computed tomography in facilitating the correct indication to coronary angiography was less relevant.

Conclusions Multidetector computed tomography is a particularly helpful technique in patients with discordance between the clinical features of chest pain and stress-test results. This technique may be introduced in the diagnostic work-up of patients with suspected coronary artery disease and may potentially reduce the number of unnecessary coronary angiography. *Coron Artery Dis* 18:265–274
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Introduction

Coronary artery disease (CAD) continues to be the leading cause of death in the United States [1] and in Europe [2]. The current American College of Cardiology/American Heart Association (ACC/AHA) guidelines [3] recommend the use of the exercise electrocardiogram (Ex-ECG) as the first test for evaluation of suspected CAD in patients able to perform exercise, with sensitivity and specificity of 68 and 77%, respectively [4]. Although exercise capacity and ST segment changes are useful prognostically, they are less accurate in detection of coronary stenoses than alternative competing stress imaging tests such as exercise echocardiogram or radio-

nuclide imaging that are often necessary [5]. The current guidelines, however, lead to some insecurity in ordering coronary angiography (CA), with an overprescription of this test; up to 25% of participants are found to have normal coronary arteries at CA [6]. One of the major arguments against this practice is the huge cost [5]. To prevent unnecessary invasive tests, the latest generations of 16 and 64-slice CT [multidetector computed tomography (MDCT)] seem to be the most promising method [7–15]. Most studies, based, however, generally on segment-based model analysis, included a small cohort of well preselected patients (e.g. exclusion of all patients with arrhythmias, even mild, those with prior known

CAD or unstable conditions, those with preserved left ventricular function), with a prevalence of CAD differing widely from that of the population normally referred to the cardiology department, and with readers blinded to the clinical history of patients [16]. Thus, they did not reflect the real clinical role of this technique.

The aim of this study was to test the accuracy of MDCT as compared with invasive CA in detecting a significant coronary stenosis in a large cohort of unselected patients referred to our hospital for coronary evaluation, testing whether cardiac-CT may facilitate the management and diagnostic work-up of patients with suspected CAD.

Methods

Study population

One hundred and forty-four patients (109 men, 35 women; mean age 61.1 ± 8.9 years) referred to our Institute to perform CA were enrolled in the study. They were selected to CA for chest pain and/or positive exercise stress test (Ex-ECG). Table 1 shows main indications for CA in the study population, including chest pain and suspected CAD (59 patients), follow-up of known CAD without significant stenosis (30 patients), coronary evaluation before thoracic surgery (12 patients), dilated cardiomyopathy of unknown etiology (27 patients) and ventricular arrhythmias (16 patients).

Study protocol and inclusion criteria

All patients referred for CA have a recent (within 15 days before admission) Ex-ECG, which was defined as positive with horizontal ST-segment depression ≥ 1.0 mm or with ascending ST-segment depression ≥ 1.5 mm or ST elevation ≥ 1.0 mm in electrocardiographic leads without Q waves.

Exclusion criteria were contraindications to the administration of iodated contrast agent, history of CAD (including previous acute myocardial infarction and coronary revascularization), severe renal insufficiency

(serum creatinine > 2 mg/dl), possible pregnancy, inability to sustain a breath-hold for 25 s, body mass index > 40 , atrial flutter with irregular ventricular rhythm or atrial fibrillation, heart rate > 75 beats/min despite β -blockade treatment. We did not exclude patients with supraventricular or ventricular premature beats or atrial flutter with regular R-wave to R-wave time interval.

According to ACC/AHA guidelines [3], 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 nitroglycerin; and typical angina defined as substernal chest pain that is exertional in nature and relieved promptly by nitroglycerin therapy. According to the nature of chest pain and the result of stress tests, the population was divided into four groups: atypical chest pain and negative stress test (group 1), typical chest pain and negative stress test (group 2), atypical chest pain but positive stress test (group 3) and typical chest pain with evidence of cardiac ischemia at stress test (group 4).

All patients gave written informed consent, and the study protocol was approved by the institutional ethical committee.

Patient preparation for multidetector computed tomography

Patients were connected to an electrocardiographic monitor before the scan and the resting heart rate was monitored. An intravenous dose of metoprolol was administered if the heart rate was > 60 beats/min or in presence of premature cardiac beats.

Scan protocol

Multidetector computed tomography was performed using a 16-slice scanner (GE Medical Systems Light Speed Pro, Waukesha, Wisconsin, USA). The scan parameters for MDCT were scan direction caudo-cranial, individual detector width 0.625 mm and gantry rotation

Table 1 Baseline characteristics of the study population

	All population	Group 1	Group 2	Group 3	Group 4
Number of patients	144	31	37	55	21
Age (years), mean \pm SD	61.9 ± 10.1	$59.1 \pm 9.9^*$	$61.7 \pm 10.3^\#$	$61.7 \pm 10.1^\S$	67.4 ± 8.1
Sex (male/female)	109/35	22/9	27/10	46/9	14/7
Clinical history					
Angina without known heart disease, n (%)	59 (41)	11 (35) [°]	22 (59) [°]	17 (31)	9 (43)
Angina with known not significant CAD, n (%)	30 (21)	0 (0) ^{°,&,@}	7 (19) [#]	14 (26)	9 (43)
Valvular disease, n (%)	12 (8)	8 (26) ^{^,&,*}	1 (3)	2 (4)	1 (5)
Dilated cardiomyopathy, n (%)	27 (19)	11 (35) ^{°,*}	6 (16)	9 (16)	1 (5)
Ventricular arrhythmia, n (%)	16 (11)	1 (3) [°]	1 (3) [°]	13 (23)	1 (5)
Beats/min before scan, mean \pm SD	78 ± 6	76 ± 4	78 ± 4	80 ± 6	78 ± 5
Number of patients receiving β -blockade, n (%)	73 (51)	15 (48)	17 (46)	31 (56)	10 (47%)
Average dose (mg) of β -blockade intravenous, mean \pm SD	8.9 ± 4.2	7.8 ± 4.1	8.1 ± 4.8	9.8 ± 3.9	8.7 ± 4.9
Beats/min during scan, mean \pm SD	61.1 ± 8.9	61.4 ± 8.7	60.3 ± 8.9	62.8 ± 8.4	57.1 ± 9.4

* $P < 0.05$ group 1 vs. group 4; $^\#P < 0.05$ group 2 vs. group 4; $^\S P < 0.05$ group 3 vs. group 4; $^\circ P < 0.05$ group 1 vs. group 2; $^\circ P < 0.01$ group 2 vs. group 3; $^\& P < 0.05$ group 1 vs. group 3; $^\@ P < 0.01$ group 1 vs. group 4; $^\wedge P < 0.01$ group 1 vs. group 2; $^\$ P < 0.01$ group 1 vs. group 3.

time 400 ms, a tube voltage of 120 to 140 kV was applied according to the patient's body weight. According to the 'ECG-pulsing technique' the tube current was modulated with a maximum current of 600 mA during a period between 40 and 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 13 mSv. Depending on the patient's heart rate, a maximum temporal resolution of 50 ms can be achieved [17,18].

A bolus of 110 ml of contrast agent (Iomeron 400 mg/ml; Bracco, Milan, Italy) was injected intravenously at 4.5 ml/s infusion rate followed immediately by a saline chaser (30 ml at 2.0 ml/s) to reduce the contrast agent volume [19] and hyperattenuation in the superior vena cava and right heart [20]. An enhancement curve was drawn by placing the region of interest on the ascending aorta at the coronary artery ostium level; as soon as the signal density level in the ascending aorta reached a predefined threshold of 200 HU units, the patient was automatically instructed to maintain an inspiratory breath-hold, while the scan started at the beginning of saline chaser infusion (average breath hold time: 21 ± 4 s).

Multidetector computed tomography image reconstruction and evaluation

Image reconstruction was retrospectively gated to the electrocardiogram including windows between 40 and 80% of the R-wave to R-wave time, at 10% intervals of cardiac cycle to minimize individual motion artifacts. Depending on the heart rate throughout the scan, axial slices were reconstructed using data from one (segment algorithm), two (burst algorithm) or four (burst-plus algorithm) consecutive heart beats.

The MDCT data sets were analyzed by three expert readers using volume rendering, multiplanar reconstruction and vessels analysis software packages (CardioQ3 package; GE Medical Systems, Waukesha, Wisconsin, USA).

Image quality was classified for each vessel as being good (no artifacts), adequate (moderate artifacts) and poor (severe artifacts). The reasons for impaired visualization were calcified plaque that precluded assessment of the coronary lumen, adjacent structures (such as contrast-enhanced ventricle or cardiac vein), motion artifacts related to high heart rate, misalignment of slices related to irregular heart beats, and image noise/suboptimal contrast enhancement. Only vessels with good or moderate quality images of all segments according to the guidelines of the American Heart Association [21] were defined assessable and considered for further analysis using a segment-based model; patients with one or more nonassessable vessels were excluded from the patient-based model.

The main coronary branches: left main, left anterior descending, first and second diagonal branches (D1 and D2), left circumflex, first and second marginal branches (M1 and M2), right coronary, and posterior descending artery with diameter of ≥ 1.5 mm, were screened for significant narrowing ($\geq 50\%$ diameter reduction). 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.

In case of disagreement among the three expert readers concerning the presence and/or severity of CAD a consensus and final decision were obtained by involving a fourth expert. This occurred only in five cases in whom consensus was determined by the majority (three out of four) who agreed in the attribution of coronary involvement.

Coronary angiography

Coronary angiography was performed according to standard techniques, and multiple views of coronary segments [21] were assessed with quantitative coronary angiography software (QCA CAAS; Pie Medical, Maastricht, The Netherlands) by an independent interventional cardiologist blinded to MDCT data. The severity of coronary stenoses was quantified on two orthogonal views, and a stenosis was classified as significant if the mean lumen diameter reduction was $\geq 50\%$.

Statistics

Statistical analysis was performed using statistical software (SPSS 11.0 for Windows; SPSS Inc., Chicago, Illinois, USA). All variables were expressed as mean \pm standard deviation. QCA was used as the 'gold standard'. Results were analyzed with a segment model according to AHA classification of coronary vessels [21] and a patient-model first including all patients regardless of segment exclusions and second excluding patients with partial coronary tree coverage owing to artifacts. Sensitivity (Se), specificity (Sp), negative predictive value (NPV), positive predictive value (PPV) and accuracy were calculated from χ^2 tests of contingency in all populations and in each group. The 95% confidence interval (CI) for all diagnostic accuracy parameters was calculated using the ratio estimator for variance derived by Rao and Scott in a segment-based model and using a conventional binomial estimator method in a patient-based model.

Moreover, quantitative lesion severity was compared between MDCT and QCA using Spearman correlation.

Results

Clinical characteristics of the patient population

Cardiac-CT was performed successfully without any complications in all 144 patients scheduled for CA. Table 1 reports clinical characteristics of the four study

groups. No differences were observed concerning the number of patients pretreated by β -blockers, the average doses of metoprolol and heart rate during the scan.

Image quality of multidetector computed tomography

According to the AHA classification of coronary vessels [21], 1801 segments out of 2160 with diameter more than 1.5 mm (83%) were included in our analysis, and 1696 out of 1801 segments (94%) were evaluable (Table 2). The main causes of artifacts were the interference of adjacent structures (37 out of 1696 segments) and suboptimal contrast enhancement (28 out of 1696 segments), particularly in small-sized segments.

Multidetector computed tomography accuracy vs. quantitative coronary angiography in a segment-based model

Multidetector computed tomography identified 258 out of 1696 segments with significant coronary stenoses, 1293 out of 1696 segments without significant coronary narrowing. The Se, Sp, NPV, PPV and accuracy in our population were 81% (95% CI 75–89%), 94% (95% CI 90–

98%), 96% (95% CI 93–98%), 75% (95% CI 69–82%) and 91% (95% CI 89–93%), respectively. MDCT was also accurate in the quantitative assessment of lesion severity; comparing the maximal percentage diameter luminal stenosis by MDCT vs. QCA, the Spearman correlation between the two techniques was 0.73 ($P < 0.01$).

Multidetector computed tomography accuracy vs. quantitative coronary angiography in a patient-based model

Multidetector computed tomography accuracy in a patient-based evaluation is summarized in Table 3. Including all patients, the Se, Sp, NPV, PPV and accuracy were 95% (95% CI 91–99%), 78% (95% CI 67–89%), 88% (95% CI 79–97%), 89% (95% CI 83–95%) and 89% (95% CI 84–94%), respectively. A complete coronary tree coverage was obtained in only 96 out of 144 patients (66%, excluding nonassessable segments). A mild, but not statistically significant, improvement in accuracy (91 vs. 89%) was observed in the analysis of this subgroup of patients (Table 3). A subanalysis of five cases with false-negative results showed one stenosis of a distal

Table 2 Image quality and artifacts of multidetector computed tomography in a segment model on the basis of the American Heart Association (AHA) segment classification [21]

Segments	No. segments > 1.5 mm, (%)	No. segments assessable, (%)	Reasons for non-assessment				
			Calcium no. (%)	Adjacent Structures no. (%)	Motion artifacts no. (%)	Misalignment of slices no. (%)	Suboptimal c.e. no (%)
LM	144 (100%)	142 (98%)	2 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
LAD proximal	144 (100%)	142 (99%)	2 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
LAD middle	144 (100%)	142 (99%)	1 (50%)	0 (0%)	1 (50%)	0 (0%)	0 (0%)
LAD distal	144 (100%)	142 (99%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (100%)
D1	88 (61%)	79 (89%)	0 (0%)	3 (33%)	1 (14%)	0 (0%)	5 (55%)
D2	37 (26%)	30 (81%)	0 (0%)	0 (0%)	0 (0%)	1 (14%)	6 (86%)
LCX proximal	144 (100%)	137 (95%)	3 (43%)	0 (0%)	2 (29%)	2 (29%)	0 (0%)
LCX middle	144 (100%)	132 (92%)	3 (25%)	8 (67%)	1 (8%)	0 (0%)	0 (0%)
LCX distal	142 (98%)	132 (92%)	0 (0%)	8 (72%)	0 (0%)	0 (0%)	2 (20%)
M1	96 (67%)	89 (93%)	0 (0%)	3 (43%)	0 (0%)	0 (0%)	4 (57%)
M2	17 (12%)	11 (64%)	0 (0%)	3 (50%)	0 (0%)	0 (0%)	3 (50%)
RCA proximal	144 (100%)	139 (96%)	0 (0%)	0 (0%)	2 (40%)	3 (60%)	0 (0%)
RCA middle	144 (100%)	130 (90%)	1 (7%)	3 (21%)	3 (21%)	7 (50%)	0 (0%)
RCA distal	144 (100%)	138 (96%)	2 (33%)	2 (33%)	2 (33%)	0 (0%)	0 (0%)
PDA	125 (87%)	111 (89%)	0 (0%)	8 (57%)	0 (0%)	0 (0%)	6 (43%)
All segments	1801 (83%)	1696 (94%)	14 (13%)	37 (35%)	12 (11%)	13 (12%)	28 (27%)

c.e., contrast enhancement; D1, first diagonal branch; D2, second diagonal branch; LAD, left anterior descending artery; LCX, left circumflex artery; LM, left main artery; M1, first marginal branch; M2, second marginal branch; PDA, posterior descending artery; RCA, right coronary artery.

Table 3 Accuracy of multidetector computed tomography (MDCT) vs. quantitative coronary angiography (QCA) in a patient-based model

MDCT vs. QCA no CAD/CAD	All population	Patients with complete coronary tree coverage	P
Number of patients, (%)	144 (100%)	96 (66%)	
True positive	90	56	n.s.
True negative	38	31	n.s.
False positive	11	5	n.s.
False negative	5	4	n.s.
Sensitivity	95% (95% CI 91–99%)	93% (95% CI 88–98%)	n.s.
Specificity	78% (95% CI 67–89%)	86% (95% CI 75–97%)	n.s.
Negative predictive value	88% (95% CI 79–97%)	89% (95% CI 79–99%)	n.s.
Positive predictive value	89% (95% CI 83–95%)	92% (95% CI 85–99%)	n.s.
Accuracy	89% (95% CI 84–94%)	91% (95% CI 85–97%)	n.s.

CAD, coronary artery disease; 95% CI, confidence interval; n.s., not significant.

Table 4 Accuracy of multidetector computed tomography (MDCT) in detection of one-, two- or three-vessel disease compared with quantitative coronary angiography (QCA) in total population

MDCT vs. QCA	QCA				Total
	Zero-vessel	One-vessel	Two-vessel	Three-vessel	
MDCT					
Zero-vessel	38	4	1	0	43
One-vessel	4	23	8	2	37
Two-vessel	6	8	20	11	45
Three-vessel	1	2	4	12	19*
Total	49	37	33	25*	144

CAD, coronary artery disease. * $P=0.054$.**Table 5 Percentage of assessable segments and accuracy of multidetector computed tomography (MDCT) versus quantitative coronary angiography (QCA) in a segment-based model in different groups**

	All	Group 1	Group 2	Group 3	Group 4
Total number of segments	2160	465	555	825	315
Number of segments > 1.5 mm (%)	1801 (84%)	392 (84%)	460 (83%)	691 (84%)	273 (87%)
Number of segments assessable (%)	1696 (94%)	381 (97%) ^{^, \$, &}	419 (91%)	642 (93%)	254 (93%)
Number of segments with CAD (%)	318 (19%)	22 (6%) ^{^, \$, &}	88 (21%) ^l	130 (20%)	78 (31%)
Accuracy	91%	94%	92%	89%	92%

[^] $P<0.01$ group 1 vs. group 2; ^{\$} $P<0.01$ group 1 vs. group 3; [&] $P<0.01$ group 1 vs. group 4; ^l $P<0.01$ group 2 vs. group 4.**Table 6 Accuracy of multidetector computed tomography (MDCT) versus quantitative coronary angiography (QCA) in a patient-based model in different groups**

	All	Group 1	Group 2	Group 3	Group 4
Total number of patients	144	31	37	55	21
Number of patient with complete coverage (%)	96 (66%)	25 (81%) [°]	25 (67%)	33 (60%)	13 (61%)
Number of patients with CAD (%)	95 (65%)	9 (29%) ^{^, \$, &}	26 (70%)	40 (72%)	20 (95%)
TP	90	8 ^{^, \$, &}	26	37	19
TN	38	21 ^{^, \$, &}	6	10	1
FP	11	1	5	5	0
FN	5	1	0	3	1
Se	95%	89%	100%	93%	95%
Sp	78%	95% ^{°, ^, &}	55%	67%	100%
NPV	88%	95% ^{&}	100%	77%	50%
PPV	89%	89%	84%	88%	100%
Accuracy	89%	94%	86%	85%	95%

[°] $P<0.05$ group 1 vs. group 3; [^] $P<0.01$ group 1 vs. group 2; ^{\$} $P<0.01$ group 1 vs. group 3; [&] $P<0.01$ group 1 vs. group 4.

segment of the left anterior descending (not treated by percutaneous transluminal coronary angioplasty), one stenosis of a marginal branch treated by percutaneous transluminal coronary angioplasty and three cases of calcified plaque determining a moderate stenosis (between 50 and 70%) not treated by percutaneous transluminal coronary angioplasty. Considering the number of narrowed vessels, MDCT seems to under-assess the number of patients without coronary disease (43 vs. 49 patients), with a tendency to underestimate three-vessel cases (19 vs. 25 patients, $P=0.054$) (Table 4).

Intragroup analysis of multidetector computed tomography feasibility and accuracy vs. quantitative coronary angiography in a segment-based model

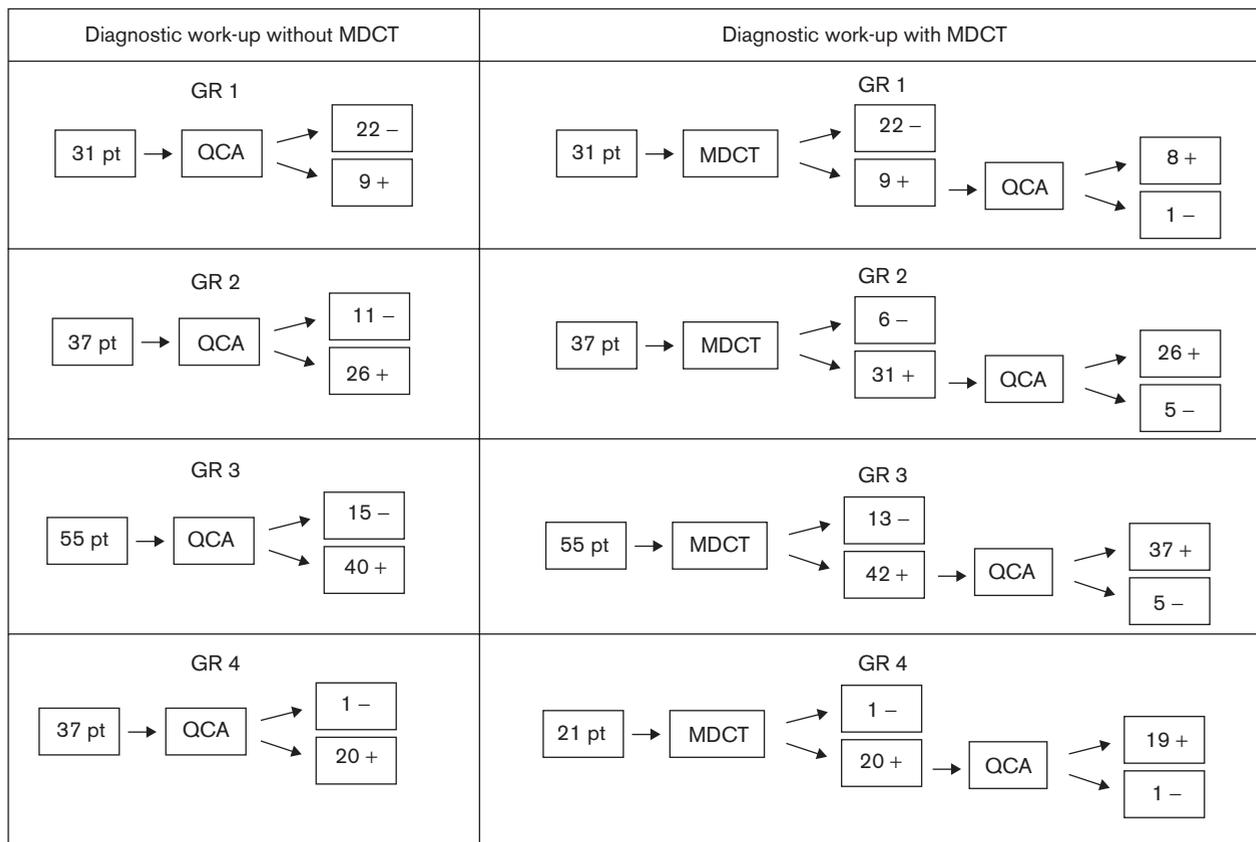
Table 5 shows that there are no differences in the feasibility and accuracy of MDCT between groups related

to the size of vessels. A higher percentage of diseased segments was detected in group 4 vs. other groups, and in groups 2 and 3 vs. group 1.

Intragroup analysis of multidetector computed tomography feasibility and accuracy vs. quantitative coronary angiography in a patient-based model

Applying a patient-based model (Table 6), group 1 shows better feasibility (25 out of 31 patients have complete coverage of the coronary tree) and a lower prevalence of CAD (nine out of 31 patients) vs. other groups, but no differences of accuracy were observed among groups. Specifically, in group 1, MDCT identified eight out of nine patients with CAD with one false-negative and one false-positive, whereas in groups 2 and 3, with an intermediate prevalence of CAD, 26 out of 26 and 37 out of 40 patients with CAD were detected, respectively.

Fig. 1



A scheme of the diagnostic work-up in the four study groups. The diagnostic work-up without multidetector computed tomography (MDCT) (left panel) leads to a significant number of potentially unnecessary invasive procedures. On the contrary (right panel), the inclusion of MDCT in the diagnostic work-up reduces cases in whom the invasive procedures were unnecessary (particularly in groups 2 and 3). QCA, quantitative coronary angiography; pt, patients.

Moreover, MDCT identified 19 out of 20 patients with CAD in group 4.

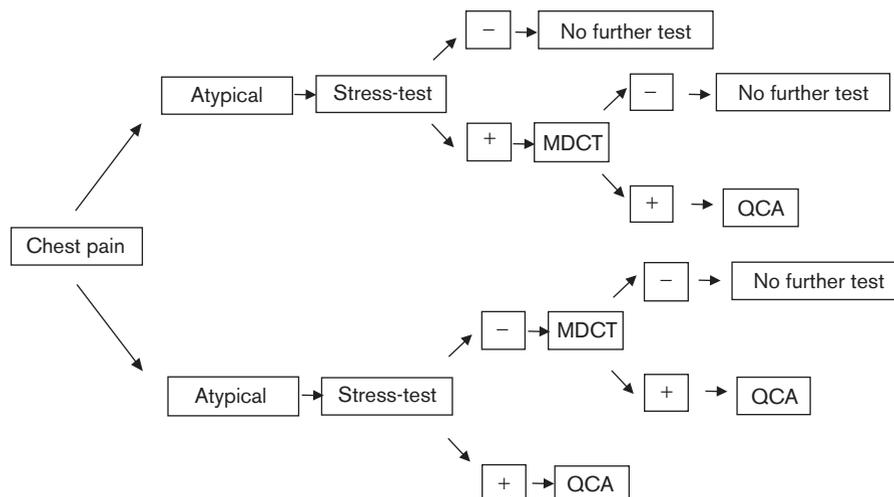
Figure 1 shows a scheme describing how MDCT may facilitate the diagnostic work-up of CAD in the four study groups and potentially reduce the number of CAs. In fact, in group 2 MDCT may avoid 16% of unnecessary CA and correctly identify significant CAD in 26 cases. In group 3, MDCT may recognize 24% of cases (13 out of 55) in whom CAs were unnecessary. On the contrary, in groups 1 and 4 the role of MDCT in the diagnostic work-up and decision-making was less relevant because clinical features and stress results were generally sufficient to correctly pose the indication to CA.

In accordance with these observations, Fig. 2 is a proposal of a diagnostic work-up flow-chart in patients with chest pain. Figure 3 shows two examples of cases in groups 3 and 2, respectively, in whom MDCT correctly excluded or detected CAD.

Discussion

The assessment of chest pain in the cardiological department is currently a major challenge and although a cardiac diagnosis may be apparent, clinical evaluation is often equivocal, resulting in a high proportion of hospital admissions [22]. With regard to this population the standard diagnostic work-up is based on clinical features, cardiovascular risk factors and stress tests [1,5,23]. Several meta-analyses have confirmed the superiority of stress imaging to the stress ECG for diagnosis of CAD [24,25]. This improvement in accuracy, however, is accompanied by greater cost and cost implications have to be considered. Kuntz *et al.* [1] have shown that in patient subgroups with a high probability of CAD, CA without previous noninvasive testing is reasonably cost-effective. Alternatively, for patients who have a very low probability of CAD the cost-effectiveness ratios of all noninvasive strategies are higher than for medical therapy [1]. The use of noninvasive testing was particularly useful in patients at moderate risk for CAD who form the 'gray-zone' in clinical decision-making. Despite these guide-

Fig. 2



A scheme that is a proposal of a diagnostic work-up including symptoms, ECG stress and multidetector computed tomography (MDCT) on the basis of the results of our study is presented. The inclusion in the diagnostic work-up of MDCT is particularly useful in cases with atypical chest pain and positive ECG stress and cases with typical chest pain and negative ECG stress. QCA, quantitative coronary angiography.

lines, up to 25% of participants are found to have normal coronary arteries at CA [6], and up to 8% of patients are inappropriately discharged from hospital with an incorrect diagnosis of noncardiac chest pain [26,27].

The introduction of 16-row and, more recently, 64-row scanners, provides promising results in the assessment of CAD [7–15]: these studies have shown high feasibility (from 84 to 100%), sensitivity (from 80 to 95%) and specificity (from 95 to 98%) but almost all of them are based on small cohorts of well-selected patients, and are based on the less clinically relevant segment model. To test the real clinical role, in our study we performed cardiac-CT in 144 consecutive nonselected patients referred to our hospital to perform a CA for suspected chest pain without previous history of significant CAD, excluding patients with absolute contraindications to MDCT (e.g. intolerance to iodated agents or atrial fibrillation). Unlike other studies [7–15], we used high doses of intravenous β -blockers in a large number of patients (51% of the population). They were administered to every patient with a heart rate over 60 beats/min, without any collateral effects. Therefore, we performed CT-scan with an average heart rate similar to that of previous studies even though the population was not selected. As our patients were not pretreated 1 h before by oral β -blockers, we needed to use high doses of intravenous metoprolol as described only by Hoffman *et al.* [9].

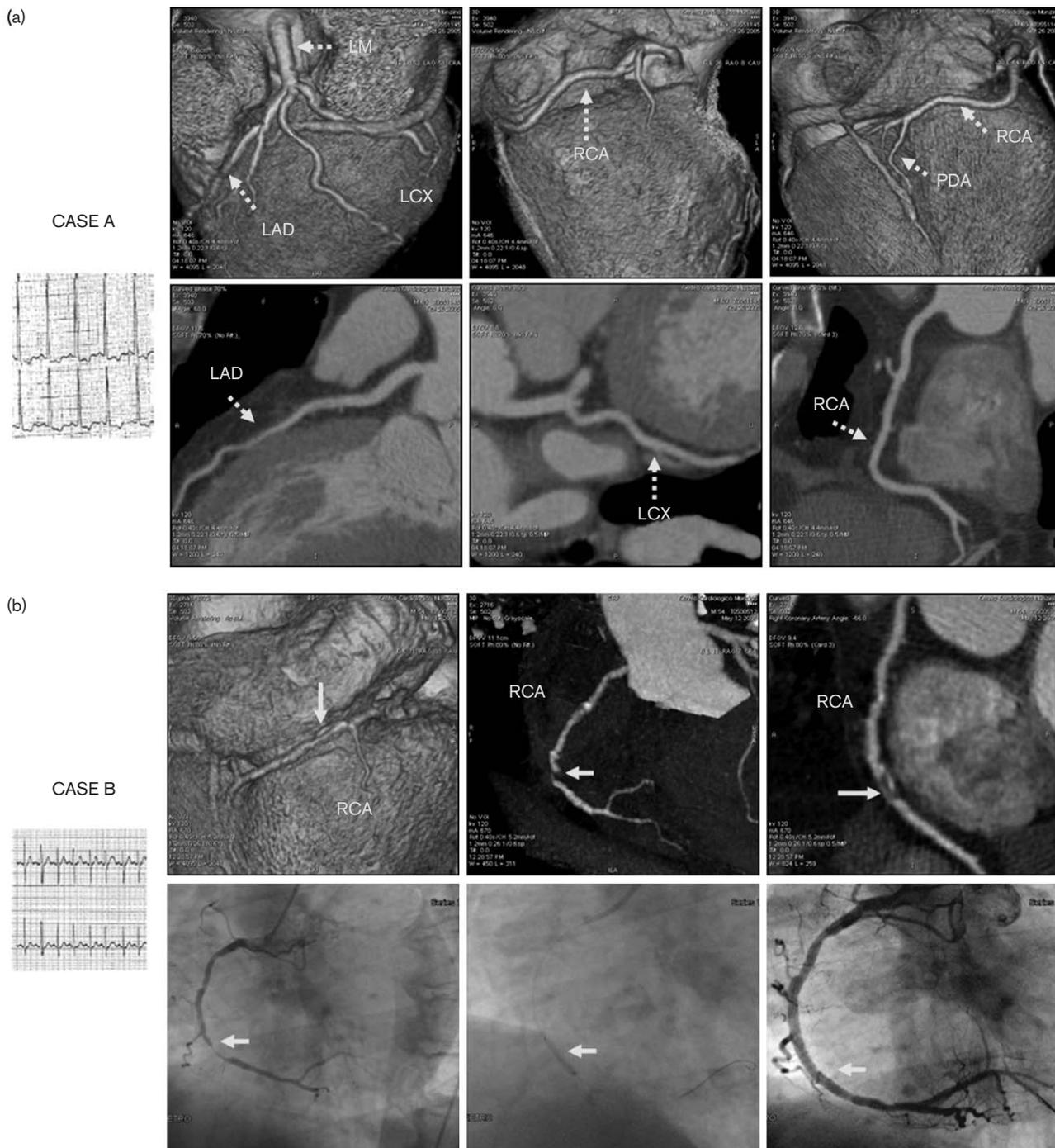
In agreement with previous studies [28–30], 305 segments out of 2160 measuring 1.5 mm or less in lumen diameter were excluded from our analysis because of spatial resolution of 16-row scanner. Nevertheless, the

exclusion of these segments, generally secondary branches as marginal and diagonal vessels did not influence the clinical role of MDCT because stenosis of these small vessels are not generally treated by revascularization procedures.

Among segments larger than 1.5 mm the number of segments assessable was high and similar to that observed in well-selected patients (1696 out of 1801 segments corresponding to 94%). The main reason for nonassessability was related to anatomical factors (35% of non-assessable segments owing to adjacent structures) and not to reasons influenced by heart rate such as motion artifacts (12 out of 1696 segments) and misalignment of slices (13 out of 1696 segments). Moreover, the visualization of main vessels was very close to 100% and most undiagnosed images concerned secondary branch because of small size (second diagonal and second marginal vessels). The accuracy of MDCT in our populations was 91%, a value that is similar to previous studies with 16-row CT [7–12] and surprisingly better than in some of studies with 64-slice CT [13–15]. This may be explained by the fact that in most studies with 64-slice CT no segments were excluded, reducing the overall accuracy of the technique.

Further considerations emerged using a more clinically relevant patient-based model. In this context, MDCT seems to be more sensitive than specific, whereas the accuracy does not change (89 vs. 91% for the segment-based model). The real limitation of a patient-based model is that in our study only 66% of the population had a complete coverage of the coronary tree and these data

Fig. 3



Two examples of cases included in groups 3 and 2. Case A: A 50-year-old woman with history of hypertension and smoking and atypical angina associated with a positive ECG stress (upper-left panel) and normal coronary arteries at multidetector computed tomography (MDCT) (upper-right panel). Case B: A 44-year-old man with typical angina and syncope during effort associated with a normal ECG stress (bottom-left panel); MDCT (bottom-right panels) showed a critical narrowing of distal RCA (arrow, first panel) treated by percutaneous transluminal coronary angioplasty and stent implantation (arrows, second and third panels). Ex-ECG, exercise electrocardiogram; LAD, left descending artery; LCX, left circumflex; LM, left main; RCA, right coronary artery; PDA: posterior descending artery.

are in agreement with the only study in which this parameter was considered [9]. The lack of one or more segments in the analysis of each patient, however, did not

significantly influence the accuracy of the technique because only minor branches were generally not visualized by the technique.

To test the improvement in the diagnostic work-up by MDCT we have evaluated the accuracy of the technique in four groups on the basis of the clinical features (characteristics of chest pain) and stress-test results. Obviously, the number of vessels over 1.5 mm does not change between groups, but it seemed that group 1 patients were more suitable for MDCT (probably because they were younger with fewer coronary calcifications). Moreover, the accuracy of MDCT in detecting significant CAD was not significantly different in the study groups even though the prevalence of CAD increased progressively from group 1 to group 4, independently of the model used.

Figure 1 shows how our clinical decision could be changed by the utilization of MDCT. In group 1, for which current guidelines suggest no further examinations after clinical evaluation and stress test, we correctly identified eight patients with CAD with only one false-negative patient, showing a better Se than clinical evaluation or stress test. In group 1, however, we also included patients with dilated cardiomyopathy, valvular disease or ventricular arrhythmias, with a higher prevalence of CAD compared with the usual prevalence of disease in patients with only atypical chest pain and negative stress test. Therefore, the use of MDCT as the sole diagnostic method in patients in whom it is mandatory to evaluate the coronary tree may be proposed.

On the contrary, in group 4, the prevalence of CAD is so high that MDCT before CA is redundant and not recommended.

The real benefits of MDCT are evident in groups 2 and 3 that form the 'gray zone' in the diagnostic flow chart of CAD. Performing CA in all patients with typical angina but no evidence of ischemia at stress test leads to 30% of unnecessary CA (11 out of 37 patients without CAD). A second-step evaluation by MDCT after stress test leads to a 16% reduction in CA (six out of 37 patients without CAD at MDCT), and including all patients subjected to CA, 16% of examinations were unnecessary. Similarly, in group 3, the evidence of cardiac ischemia makes CA mandatory in these patients, but 15 out of 55 patients have a normal coronary tree (27%). A preliminary CT evaluation would have avoided CA in 13 out of 55 patients (reduction of 24%). Even though in this group we have three false-negative results at MDCT, these patients had border-line stenoses at CA (between 50 and 65% of narrowing) and they did not undergo angioplasty. These results are in agreement with a very recent study by Dewey *et al.* [31] that showed in a consecutive series of patients scheduled to undergo conventional CA, the performance of MDCT for diagnosis of CAD was superior to that of stress ECG.

Limitations of the study

We did not include in our analysis results of other stress tests (echo stress or nuclear testing) that may have a higher overall accuracy in comparison with ECG stress alone. ECG stress, however, is still utilized to select patients for CA and continues to be the most commonly applied noninvasive test for diagnosis of CAD. Moreover, other stress tests may also show discrepancies between typical or atypical symptoms and results in several cases. Even though our data may not exclude that the inclusion of other imaging modalities would have been able to better stratify CAD, our observations suggest a more appropriate use of MDCT in association with a standard first line test such as ECG stress.

The second limitation of the study is the use of 16-slice CT that is superseded by the new-generation scanner. The improvement of accuracy with 64-slice CT, however, could further reinforce the clinical conclusion of this paper, through a more precise detection of coronary stenoses and evaluation of small branches.

Our population included cases with a marked prevalence of males (male/female ratio of 3:1) related to the prevalence of the disease in our consecutive series. Further studies including larger numbers of patients are needed to evaluate whether MDCT in male and female subgroups may have different diagnostic impact.

Conclusions

Our data suggest that MDCT is feasible and accurate in a nonselected population with suspected CAD. This technique is particularly useful in patients with intermediate risk and discordance between the characteristics of chest pain and stress-test results. MDCT may be introduced in the diagnostic work-up of unselected patients with suspected CA and may potentially reduce the number of unnecessary CA, facilitating the correct identification of significant coronary stenoses.

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