64-Slice CT coronary angiography in patients with non-ST elevation acute coronary syndrome

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Background: A high diagnostic accuracy of 64-slice CT coronary angiography (CTCA) has been reported in selected patients with stable angina pectoris, but only scant information is available in patients with non-ST elevation acute coronary syndrome (ACS).

Objectives: To study the diagnostic performance of 64-slice CTCA in patients with non-ST elevation ACS.

Patients and methods: 64-slice CTCA was performed in 104 patients (mean (SD) age 59 (9) years) with non-ST elevation ACS. Two independent, blinded observers assessed all coronary arteries for stenosis, using conventional quantitative angiography as a reference. Coronary lesions with $\geq 50\%$ luminal narrowing were classified as significant.

Results: Conventional coronary angiography demonstrated the absence of significant disease in 15% (16/104) of patients, and the presence of single-vessel disease in 40% (42/104) and multivessel disease in 44% (46/104) of patients. Sensitivity for detecting significant coronary stenoses on a patient-by-patient analysis was 100% (88/88; 95% CI 95 to 100), specificity 75% (12/16; 95% CI 47 to 92), and positive and negative predictive values were 96% (88/92; 95% CI 89 to 99) and 100% (12/12; 95% CI 70 to 100), respectively.

Conclusion: 64-slice CTCA has a high sensitivity to detect significant coronary stenoses, and is reliable to exclude the presence of significant coronary artery disease in patients who present with a non-ST elevation ACS.

Patients with a non-ST elevation acute coronary syndrome (ACS) are usually stratified into high and low risk for progression to myocardial infarction or death on the basis of their clinical presentation, ECG changes, biomarkers, electrical or haemodynamical instability, and presence of diabetes mellitus.¹ An invasive management strategy, including conventional coronary angiography (CCA) and revascularisation, is recommended in high-risk patients, whereas a conservative strategy with ischaemia-guided revascularisation is recommended in low-risk patients.^{1–3} We investigated the feasibility and diagnostic accuracy of 64-slice CT coronary angiography (CTCA) in 104 patients with non-ST elevation ACS as a first step to evaluate the potential decision-making role of CT in this patient cohort.

METHODS

Study population

Over a 12-month period, we included 104 patients presenting with unstable angina pectoris or non-ST-segment elevation myocardial infarction. They were stratified as either at high or low risk according to the current European guidelines, on the basis of baseline characteristics, troponin rise or ECG changes.¹ High-risk patients and low-risk patients with a positive or inconclusive exercise ECG test or high suspicion for obstructive coronary artery disease (CAD) underwent both CTCA and CCA. Furthermore, patients presenting with an ST-segment elevation myocardial infarction were not included, but were immediately referred for direct percutaneous coronary intervention (PCI). No patients with previous history of PCI or coronary artery bypass graft (CABG), impaired renal function (serum creatinine $>120 \mu\text{mol/l}$), known intolerance to iodinated contrast material and atrial fibrillation were included. All patients underwent CCA, which was the standard of reference. The

institutional review board of Erasmus MC Rotterdam approved the study and all subjects gave informed consent.

Patient preparation

Patients with a heart rate >65 bpm before the examination received additional β blockers (50/100 mg Metoprolol), and all were given thorough breath-hold instructions.

Scan protocol

All scans were made with a 64-slice CT scanner, which had a gantry rotation time of 330 ms, a temporal resolution of 165 ms and a spatial resolution of 0.4 mm^3 (Sensation 64, Siemens, Forchheim, Germany). Initially, a calcium scan was performed using standardised scan parameters $64 \times 0.6 \text{ mm}$ collimation, 330 ms rotation time, 3.8 mm/rotation table feed, 120 kV tube voltage, 150 mA tube current and prospective x ray tube modulation. Then the CTCA was completed, which had similar parameters except for a higher tube current of 900 mA and absence of x ray tube modulation. The radiation exposure for CTCA using this scan protocol was calculated as 15.2–21.4 (male/female) mSv using dedicated software (WinDose, Institute of Medical Physics, Erlangen, Germany). The radiation exposure for calcium scoring using a comparable scan protocol (including prospective x ray tube modulation) on a 16-slice scanner was calculated as 1.3–1.7 (male/female) mSv.⁴

A bolus of 80–100 ml of contrast material (400 mgI/ml; Iomeron, Bracco, Milan, Italy) was injected intravenously in an antecubital vein at a flow rate of 5 ml/s. A bolus-tracking

Abbreviations: ACS, acute coronary syndrome; CABG, coronary artery bypass graft; CAD, coronary artery disease; CCA, conventional coronary angiography; CTCA, CT coronary angiography; PCI, percutaneous coronary intervention; QCA, quantitative coronary angiography

technique was used to synchronise the arrival of contrast in the coronary arteries, and the scan was started once the contrast attenuation in a preselected region of interest in the ascending aorta had reached a predefined threshold of +100 HU.

Image reconstruction

Images were obtained during a half x ray tube rotation, resulting in an effective temporal resolution of 165 ms. Datasets were reconstructed immediately after the scan. To obtain optimal image quality, datasets were reconstructed in the mid-to-end diastolic phase using retrospective ECG gating with an absolute reverse or percentage technique as described previously by Mollet.⁵ In case of impaired image quality due to motion artefacts or breathing artefacts, additional reconstructions were made in the end-systolic phase.

Quantitative coronary angiography

All CT scans were carried out within 1–2 days of performing CCA. One experienced cardiologist, blinded to the results of CTCA, identified and analysed all coronary segments, using a 17-segment modified American Heart Association (AHA) classification.⁶

All segments, regardless of size, were included for comparison with CTCA. Segments were classified as normal (smooth parallel or tapering borders), as having non-significant disease (wall irregularities or <50% stenosis) or as having significant disease (stenosis ≥50%). Stenoses were evaluated in the worst view, and were classified as significant if the reduction in lumen diameter exceeded 50% of that measured by the validated quantitative coronary angiographic (QCA) algorithm (CAAS, Pie Medical, Maastricht, The Netherlands).

CT image evaluation

One observer analysed the total calcium scores of all patients using the appropriate software (Syngo, Calcium Scoring, Siemens Fonchheim, Germany), expressing results as an Agatston score.⁷ Two experienced observers, a radiologist and a cardiologist, all unaware of the results of CCA, evaluated the CTCA datasets on an offline workstation (Leonardo, Siemens, Forchheim, Germany). The axial slices were initially evaluated for the presence of significant segmental disease and, additionally, multiplanar and curved multiplanar reconstructed images were used. Segments located distally to a chronic total occlusion were excluded because of poor distal filling by collaterals. Interobserver disagreements were resolved by a third reader.

Statistical analysis

The diagnostic performance of CTCA for detecting significant stenoses in the coronary arteries using QCA as the standard of reference is presented in terms of sensitivity, specificity, positive predictive value and negative predictive values with the corresponding 95% CIs. Positive (sensitivity/(1–specificity)) and negative ((1–sensitivity)/specificity) likelihood ratios are given. The likelihood ratio incorporates both the sensitivity and specificity of a test and provides a direct estimate of how much a test result will change the odds of having a disease. Post-test odds can be calculated by multiplying the pre-test odds by the likelihood ratios. Comparison between CTCA and QCA was performed on three levels of analysis: patient by patient, vessel by vessel and segment by segment. To investigate the effect of nesting, an additional sensitivity analysis was done; repeated assessments (segment by segment and vessel by vessel) within

Table 1 Patient demographics (n= 104)

	Low risk	High risk
n	33	71
Mean (SD) age, range (years)	58 (7), (38–75)	59 (10), (30–84)
Males	23 (70)	52 (73)
Mean (SD) calcium score*	473.9 (738.2)	440.0 (513.6)
Mean (SD) BMI†	25.8 (3.6)	26.5 (3.7)
Recurrent ischaemia‡	—	49 (71)
Early post-infarct unstable angina	—	9 (13)
Elevated troponin levels	—	55 (78)
Diabetes mellitus	—	9 (13)
Normal ECG	21 (64)	—
ECG with negative or flat T-waves	12 (36)	—
Positive exercise ECG test	23 (70)	—
Inconclusive exercise ECG test	3 (9)	—
Highly suspicious for obstructive CAD	7 (21)	—
Traditional risk factors		
Hypertension	17 (52)	37 (52)
Hypercholesterolaemia	22 (67)	40 (56)
Diabetes mellitus	0 (0)	9 (13)
Smoker	14 (42)	35 (49)
Ex-smoker	2 (6)	2 (3)
Family history of CAD	24 (73)	32 (45)
Obese‡	8 (24)	15 (21)
Previous myocardial infarction	1 (3)	17 (24)
Conventional angiography		
Absence of coronary disease	2 (6)	2 (3)
Non-significant disease	3 (9)	9 (13)
Single-vessel disease	15 (45)	27 (38)
Two-vessel disease	10 (30)	26 (37)
Three-vessel disease	3 (9)	7 (10)

BMI, body mass index; CAD, coronary artery disease.
Values are n (%) unless otherwise indicated.
According to European Society for Cardiology guidelines, patients were stratified into high and low-risk groups, which give a risk estimate for progression to myocardial infarction or death.
*Agatston score.
†BMI ≥30 kg/m².
‡Recurrent ischaemia defined as either recurrent chest pain or dynamic ST-segment changes (in particular, ST-segment depression or transient ST-segment elevation).

Table 2 Diagnostic performance and predictive value of 64-slice CTCA for the detection of $\geq 50\%$ stenosis on quantitative coronary angiography

	Prevalence of disease, %	n	TP	TN	FP	FN	κ	Sensitivity, % (95% CI)	Specificity, % (95% CI)	PPV, % (95% CI)	NPV, % (95% CI)	+LR	-LR
All patients	85	104	88	12	4	0	0.84	100 (95 to 100)	75 (47 to 92)	96 (89 to 99)	100 (70 to 100)	4.00	0.00
High risk	85	71	60	8	3	0	0.82	100 (93 to 100)	73 (39 to 93)	95 (86 to 99)	100 (60 to 100)	3.67	0.00
Low risk	85	33	28	4	1	0	0.87	100 (85 to 100)	80 (30 to 99)	93 (80 to 100)	100 (40 to 100)	5.00	0.00
Vessel-based analysis													
All vessels	35	416	141	214	58	3	0.70	98 (94 to 99)	79 (73 to 83)	71 (64 to 77)	99 (96 to 100)	4.59	0.03
RCA	48	104	48	39	15	2	0.68	96 (85 to 99)	72 (58 to 83)	76 (64 to 86)	95 (82 to 99)	3.46	0.06
LM	3	104	3	98	3	0	0.65	100 (31 to 100)	97 (91 to 99)	50 (14 to 86)	100 (95 to 100)	33.67	0.00
LAD	47	104	49	32	23	0	0.57	100 (91 to 100)	58 (44 to 71)	68 (56 to 78)	100 (87 to 100)	2.39	0.00
CX	39	104	40	46	17	1	0.66	98 (86 to 100)	73 (60 to 83)	70 (56 to 81)	98 (87 to 100)	3.62	0.03
Segment-based analysis													
All segments	13	1525	183	1205	122	15	0.68	92 (88 to 96)	91 (89 to 92)	60 (54 to 65)	99 (98 to 99)	10.05	0.08
Proximal	14	416	58	312	44	2	0.65	97 (87 to 99)	88 (84 to 91)	57 (47 to 67)	99 (97 to 100)	7.82	0.04
Mid	23	302	67	199	34	2	0.71	97 (89 to 99)	85 (80 to 90)	66 (56 to 75)	99 (96 to 100)	6.65	0.03
Distal	9	327	24	286	11	6	0.71	80 (61 to 92)	96 (93 to 98)	69 (51 to 83)	98 (95 to 99)	21.60	0.21
Side branch	8	480	34	408	33	5	0.60	87 (72 to 95)	92 (90 to 95)	51 (38 to 63)	99 (97 to 100)	11.65	0.14

CTCA, CT coronary angiography; FN, false negative; FP, false positive; LAD, left anterior descending coronary artery; LCx, circumflex coronary artery; LM, left main coronary artery; +LR, positive likelihood ratio; -LR, negative likelihood ratio; NPV, negative predictive value; PPV, positive predictive value; RCA, right coronary artery; TP, true positive; TN, true negative.

According to the 17-segment modified American Heart Association (AHA) classification, 1525 segments and 416 vessels visualised with conventional coronary angiography were included for segment and vessel analysis.

the same patient were made, which were not independent observations. Interobserver and intraobserver variabilities for the detection of significant coronary stenosis and agreement between techniques to classify patients as having no, single or multi-vessel disease were determined using κ statistics.

RESULTS

Table 1 shows the patient demographics. In all, 86% (89/104) of the patients received oral β -blockers as treatment for ACS. Additional β -blockers were administered in 63% (65/104) of patients, and the mean (SD) heart rate dropped within 60 min from 66 (9) to 60 (8) bpm in these patients. The mean (SD) scan time was 12.3 (1.2) s. As a first step, all datasets were reconstructed in the mid-to-end diastolic phase. In 34% (35/104) of cases, additional higher quality end-systolic reconstructions were used.

Diagnostic performance of 64-slice CT coronary angiography: patient-by-patient analysis

The prevalence of significant CAD, defined as having at least one $\geq 50\%$ stenosis per patient, was 85%. Table 2 details the diagnostic performance of CTCA for detecting significant stenoses on a patient-based analysis. The diagnostic accuracies of patients in the low- and high-risk groups were similar.

Twelve patients with either an angiographically normal CCA⁴ or a non-significant disease⁸ were correctly identified with CT. However, two patients with only wall irregularities on the CCA were incorrectly classified as having single-vessel disease on the CT scan and two patients as having multi-vessel disease. All 88 patients with significant CAD on CCA were correctly identified on the CT scan (figs 1 and 2). However, in 23 patients with single-vessel disease on CCA, CTCA overestimated the severity of additional lesions, which resulted in their incorrect classification as having multi-vessel disease on CTCA. In all, 27 patients in the low-risk group underwent PCI, 1 underwent CABG and 5 were treated medically. In the high-risk group, 55 underwent PCI, 5 underwent CABG and 11 were treated medically. Agreement between CTCA and QCA on a per-patient (no or any disease) level was very good (κ value 0.84), whereas agreement between techniques to classify patients as having no, single and multi-vessel disease was moderate (κ value 0.55).

Diagnostic performance of 64-slice CTCA: vessel-by-vessel analysis

Table 2 details the diagnostic performance of CTCA for the detection of significant lesions in a vessel-based analysis. Two significantly diseased right coronary arteries and one diseased circumflex coronary artery were incorrectly classified as non-significantly diseased on the CT scan. Out of a total of 416 vessels, 59 non-obstructive vessels were overestimated and scored as false positives. Agreement between CTCA and QCA on a per-vessel level was good (κ value 0.70).

Diagnostic performance of 64-slice CTCA: segment-by-segment analysis

A total of 1525 segments were included for comparison with QCA. Potentially, 17 segments per patient can be presented for analysis. A total of 243 segments were not visualised on the CCA. A total of 181 segments were excluded owing to variations in coronary anatomy, and 62 segments owing to the presence of a proximal occlusion and poorly filled distal segments by collaterals. All segments were included, irrespective of the presence of calcifications or poor image quality. Interobserver and intraobserver variabilities for detection of a significant stenosis per segment had a κ value of 0.69 and 0.73, respectively. Table 2 details the diagnostic performance of

Figure 1 This patient with prior history of a mitral valve plasty for endocarditis was admitted with a non-ST segment elevation myocardial infarction. A volume-rendered CT coronary angiography image (A) reveals the anatomy of the right coronary artery. Two curved multiplanar reconstructed images (C, D) disclose a significant stenosis (arrow) in the proximal right coronary artery, which was corroborated by conventional coronary angiography (B).

CTCA for detecting significant stenoses. Agreement between CTCA and QCA on a per-segment level was good (κ value 0.68).

Fifteen significant coronary stenoses were underestimated or missed and classified as non-significant. Most of these significant lesions (11/15) were located in distal segments or in side branches. In all, 123 non-significant lesions were detected with CTCA, but the severity of these stenoses was overestimated. This overestimation, in 67% (83/123) owing to heavy calcification, resulted in incorrect classification as significant stenoses on the CT scan. Patients were divided into tertiles on the basis of the mean calcium score. The presence of calcium decreased the diagnostic accuracy (low calcium score 0.95, mid 0.89 and high 0.88; table 3).

To exclude the possible confounding effect of nesting, random selection of a single segment per patient was performed. The diagnostic accuracy for detecting significant CAD was a sensitivity of 93% (13/14; 95% CI 64 to 100), a specificity of 93% (84/90; 95% CI 93 to 97), a positive predictive value of 68% (13/19; 95% CI, 43 to 86) and a negative predictive value of 99% (84/85; 95% CI 93 to 100).

DISCUSSION

Several recent reports about the diagnostic performance of 64-slice CTCA have shown a high sensitivity and a negative predictive value to detect or exclude the presence of significant coronary stenosis in patients scheduled for CCA.^{5 8-14} However,

only scant information is available about the diagnostic performance of CTCA in a limited number of patients with ACS.^{5 8 15 16}

In our study, the prevalence of obstructive CAD was 85%, which was in keeping with previous reports evaluating ACS angina syndromes.^{2 3 17-19} In this high pre-test risk population, we demonstrated a high diagnostic accuracy in patients with non-ST elevation ACS. In segments where interpretation was difficult owing to heavy calcification, there was a tendency for observers to score these as positive for significant stenosis in order to reduce the chance of missing an important lesion. This “defensive scoring” approach is also likely to be used in clinical practice when evaluating symptomatic patients. The high negative predictive value of the CT scan despite significant coronary calcification and the high prevalence of CAD demonstrates that significant CAD can be ruled out in this patient group.

Patients with non-segment elevation ACS classified as at high risk on the basis of baseline characteristics, troponin or ECG changes are best managed with an invasive strategy.¹⁻³ These patients should generally undergo a CCA followed by revascularisation, if appropriate, in the first few days after admission to hospital. The role of CTCA in these patients is not just for the detection of significant disease; the detailed delineation of coronary anatomy may also be useful to guide subsequent management. In this study, the agreement between CTCA and QCA in the classification of patients as having no,

Figure 2 A maximum intensity projected CT coronary angiography image shows a large non-calcified plaque in the proximal segment of the right coronary artery (A). Two curved multiplanar reconstructed images (C, D) disclose the high-grade stenosis, confirmed by conventional coronary angiography (B).

single or multi-vessel disease was moderate. This is due to the relatively high number of false positive segments scored predominantly because of calcification. In 41 out of the 104 patients, at least one vessel was overestimated as having a significant stenosis. Given this current limitation, CTCA may need to evolve further before it can more accurately guide future management, in particular either percutaneous or surgical revascularisation, in these high-risk patients. At the moment, even though the results are promising, a clinical role of CTCA in these high-risk patients is not defined.

Currently, CTCA may be more suited in the low-risk non-segment-elevation ACS group. These patients, without recurrent chest pain or evidence of myocardial necrosis, are recommended to undergo a stress test after an observation period. CCA is recommended in these patients only if significant ischaemia is demonstrated during stress testing.¹ However, stress testing, particularly treadmill or bicycle stress testing, may be inconclusive. The role of CTCA may be to replace the stress test as the first investigation in this population group. Given the excellent negative predictive value as demonstrated in this study, a negative CTCA would allow patients to be discharged and other non-cardiac causes of the presenting chest pain to be considered. Patients with non-obstructive CAD on CTCA would continue to be managed medically, including appropriate secondary prevention, and the need for future stress testing or CCA would depend on further symptoms.

Patients with significant disease on CTCA in this patient group could be referred directly for CCA, particularly if there was left main disease, three-vessel or proximal segment disease of a main coronary artery. Patients with small-vessel disease

(ie, distal disease <2 mm), equivocal lesions or uninterpretable scans could undergo a stress test to further guide the need for CCA. However, the use of sequential testing is controversial, as no data are available showing better test results than a stress test alone.

LIMITATIONS OF THE STUDY

We did not include patients with severe ongoing ischaemia, or haemodynamic or electrical instability, to prevent further delays of revascularisation treatment. Furthermore, inclusion comprised a non-consecutive group of patients. Owing to logistic reasons, it was not feasible to scan and include every patient presenting with a non-ST elevation ACS. Moreover, patients in the low-risk group with a negative exercise ECG test were not included, since these patients did not receive a CCA.

Heart rate reduction with β -blockers is standard practice in patients presenting with a non-ST elevation ACS. Additional β -blockers were given to reduce the heart rate even more in order to achieve optimal heart rate control. With the next generation dual-source CT scanners, scanning at higher heart rates will be possible owing to the improved temporal resolution of 83 ms.^{20 21}

The rather high radiation exposure of CTCA as compared with CCA is of concern.^{22 23} The radiation exposure can be reduced by 40% using the prospective x ray tube current modulation. However, this limits the possibility to reconstruct valuable datasets during the end-systolic phase.

The presence of atrial fibrillation precludes the use of CTCA and was one of the exclusion criteria.

Table 3 Influence of coronary calcifications on the diagnostic accuracy of 64-slice CT coronary angiography on a segment-based analysis

Calcium score	Patients, n	Segments, n	Mean (SD), (range) Agatston Score	TP	TN	FP	FN	κ	Sensitivity, % (95% CI)	Specificity, % (95% CI)	PPV, % (95% CI)	NPV, % (95% CI)	+ LR	– LR
First tertile	35	530	30 (34) (0–105)	42	465	20	3	0.76	93 (81 to 98)	96 (94 to 97)	68 (55 to 79)	99 (98 to 100)	22.63	0.07
Second tertile	35	505	266 (81) (107–375)	57	394	47	7	0.62	89 (79 to 95)	89 (86 to 92)	55 (45 to 64)	98 (96 to 99)	8.36	0.12
Third tertile	34	490	1073 (665) (400–2870)	84	346	55	5	0.66	94 (87 to 98)	86 (82 to 89)	60 (52 to 69)	99 (97 to 99)	6.88	0.07

FN, false negative; FP, false positive; LAD, left anterior descending coronary artery; +LR, positive likelihood ratio; –LR, negative likelihood ratio; NPV, negative predictive value; PPV, positive predictive value; TP, true positive; TN, true negative.

CONCLUSIONS

The 64-slice CT angiography has a high sensitivity to detect significant coronary stenoses and is reliable to exclude the presence of significant CAD in patients who present with a non-ST elevation ACS. The role of CTCA in these patients, particularly in the low-risk group, needs to be further evaluated.

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IMAGES IN CARDIOLOGY

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An unexpected finding during planned primary percutaneous coronary angioplasty

A 65-year-old woman presented with acute central chest pain. Her ECG showed inferior ST elevation and she was transferred to our cardiac catheterisation laboratory for primary percutaneous coronary intervention. Coronary angiography showed no obstructive coronary atheroma, though a foreign body appeared to be lodged within the heart (panel A). The following morning her troponin T level was raised at 1.15 ng/ml.

A Port-O-Cath had previously been inserted via the right subclavian vein as part of the treatment of breast carcinoma. Thoracic CT demonstrated a fragment of the catheter lying across the fossa ovalis. There was no evidence of pulmonary thromboembolism or recurrence of the breast carcinoma. Transoesophageal echocardiography suggested thrombus was adherent to the fragment within the right atrium. After 1 week's treatment with heparin, thrombus was still visible. As we considered percutaneous retrieval might cause systemic embolism, the fragment was removed under direct visualisation through a longitudinal right atriotomy while the patient was on cardiopulmonary bypass (panel B). At

Coronary angiogram: right anterior oblique projection demonstrating the embolised venous catheter fragment within the atria.

operation, most of the catheter fragment was seen within the left atrium without any visible thrombus attached; the patent foramen ovale was repaired and the remainder of the Port-O-Cath removed. The patient has remained asymptomatic.

Catheter fracture usually results from compression of implanted catheters lying

Hub port and catheter after removal; centimetre scale rule for reference.

between the first rib and the clavicle. We suspect that the acute presentation was secondary to paradoxical thromboembolism to the coronary circulation. As far as we know, this is the first report of migration of a fractured venous catheter across a patent foramen ovale resulting in acute myocardial infarction.

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