Original article

Diagnostic accuracy of Computed Tomography Coronary Angiography in a high risk symptomatic population

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Abstract. *Objective:* To evaluate the diagnostic accuracy of 64-slice computed tomography (CT) coronary angiography (CA) for the detection of significant coronary artery stenosis (≥50% lumen reduction) as compared to invasive coronary angiography (ICA) in a population of patients with chest pain and high risk. **Materials and methods:** 44 patients (30 male; mean age 60.2±12.1yrs) with chest pain were prospectively enrolled. In patients with heart rate ≥70 bpm an oral dose of 100 mg of β-blocker was administered. For CT-CA (Sensation 64, Siemens, Germany) an intravenous bolus of 100 ml of iodinated contrast material (Iomeron 400, Bracco, Italy) was injected. The average scan time was 13.3±0.9s. Two observers evaluated CT-CA vs. ICA as a reference standard for the detection of significant (≥50% lumen reduction) coronary artery stenosis. *Results:* ICA demonstrated the absence of coronary artery disease (CAD) in 13.6% of the patients (6/44), the presence of non significant CAD 4.6% (2/44), single vessel disease in 27.2% (12/44) and multi-vessel disease in 54.6% (24/44) of the patients. None of the patients was excluded from the study population. Ninety-three significant obstructive coronary lesions were observed. Sensitivity, specificity, positive and negative predictive value of CT-CA were 98.6% (70/71), 92.4% (97/105), 89.7% (70/78) and 99% (97/98), respectively. All patients with at least one significant coronary lesion were correctly identified by CT-CA. *Conclusions:* CT-CA is a reliable alternative to ICA in a selected population of patients with chest pain and high risk. (www.actabiomedica.it)

Key words: Multislice Computed Tomography, Invasive Coronary Angiography, Coronary Artery Disease, Diagnostic Accuracy, High Risk

Introduction

The latest technological advances in Computer Tomography technology allow non-invasive coronary angiography imaging (CT-CA) providing a high diagnostic accuracy for the detection of coronary artery stenosis (1-17).

With 64-slice CT scanners, the higher performance of x-ray source (tube) and sensitivity of the detectors result in an improved temporal resolution of 330ms and an isotropic spatial resolution, respectively, with minimal residual-motion artefacts (1-17).

The aim of the study is to assess diagnostic accuracy of non-invasive coronary angiography with 64-slice CT-CA in the detection of ≥50% stenosis in 44 high risk symptomatic patients.

Materials e Methods

Patient population

We enrolled in the study 44 patients (30 male and 14 female; mean age 60.2±12.1 yrs) with chest pain

Table 1. Patients' characteristics.

	Total	Gender	
		Males	Females
Population			
Number of patients	44	30	14
Age (mean±SD)	60.2±12.1	59.2±12.9	62.4±10.4
Symptoms			
Stable Angina (%)	26 (59.1)	15 (35.7)	9 (64.3)
Atypical chest pain	2 (4.5)	1 (2.4)	1 (7.1)
ACS	13 (29.5)	9 (21.4)	4 (28.6)
- Unstable Angina	6 (13.6)	6 (14.3)	0 (0)
- AMI	10 (22.7)	6 (14.3)	4 (28,6)
Cardiovascular Risk Factors			
Hypertension	14 (31.8)	7 (16.7)	5 (35.7)
Hypercholesterolemia	32 (72.7)	19 (45.2)	11 (78.6)
Diabetes	7 (15.9)	0 (0)	3 (21.4)
Smoke	13 (29.5)	8 (19)	4 (28.6)
Family history	10 (22.7)	6 (14.3)	2 (14.3)
Obesity (BMI ³ 30 Kg/m^2)	13 (29.5)	9 (21.4)	3 (21.4)
Calcium score (Agatston-score)	509.8±606.8	556.9±675.7	408.7±427.9
Reason for CT-CA			
Pre-CABG	14 (31.8)	10 (33.3)	4 (29)
Pre-PCI	30 (68.2)	20 (66.6)	10 (71)

Abbreviations: SD = Standard Deviation; ACS = Acute Coronary Syndrome; AMI = Acute Myocardial Infarction; BMI= Body Mass Index; PCI= Percutaneous Coronary Intervention; CABG = Coronary Artery Bypass Surgery.

(atypical angina, typical/stable angina, unstable angina or acute coronary syndrome), who were referred for invasive ICA (Table 1). All patients underwent first 64-slice CT-CA and then ICA.

Inclusion criteria for the CT scan were: indication for ICA, sinus rhythm, and the ability to perform a breath-hold of at least 12s.

Exclusion criteria were previous Percutaneous Coronary Intervention (PCI) with stenting or Coronary Artery Bypass Graft (CABG).

Patients with acute coronary syndrome in which the CT scan would have determined a delay in the reperfusion treatment (primary PCI) and the ones with absolute contra-indications for the administration of iodinated contrast-agent (i.e. allergy, kidney failure or thyroid disease) were also excluded.

This study was approved by the local Ethics Committee and all patients gave their informed consent.

Patient preparation

In patients with heart rate ≥70 bpm, we administered a single oral dose of 100 mg of metoprolol (Selokeen®, AstraZeneca Pharmaceutics, UK) in the absence of contra-indications. The dose was repeated when deemed necessary. Also an oral dose of 1 mg of lorazepam (Temesta®, Wyeth-Ayerst, NL) was administered when the psychological component of heart rate was present.

Image acquisition protocol and reconstruction

A 64-slice clinical CT scanner was used for the study (Sensation 64, Siemens, Forchheim, Germany) (18). Prior to CT-CA, all patient underwent standard calcium scoring protocol to allow the quantification of the amount of calcification within the coronary artery tree.

Scans parameters used for calcium scoring scan were: number of detector lows 20x1.2 mm, gantry rotation time 330 ms, pitch 0.2, tube voltage 120 kV, tube current 150 mAs. The image reconstruction parameters were: effective slice thickness 3 mm, increment 1.5 mm, a field of view (FOV) 150-180 mm, a Calcium Score convolution filter dedicated. The temporal window was locked at 60% of R-R Interval.

Scans parameters used for coronary angiography CT were: number of detector lows 32x2x0.6 mm, individual detector width 0.6 mm, gantry rotation time 330 ms, table feed per rotation 3.84 mm (pitch 0.2), tube voltage 120 kV, tube current 900 mAs, slice thickness 0.6-0.75 mm, increment 0.4 mm, a field of view (FOV) 150-180 mm, a medium smooth convolution filter. The temporal window was locked at 60% of R-R Interval. We did not use ECG-gated prospective acquisition.

The estimated radiation dose applied during angiography examination (mean 15/21mSv for male/female) was calculated using a dedicated software (WinDose®, Institute of Medical Physics, Erlangen, Germany).

The double focal spot technology along z-axis (i.e. flying focal spot) allows to combine two overlapping sets of 32x06 mm measurements to create 64 projections along the z-axis, per gantry rotation, with an overlap of 0.3 mm for each 0.6 mm measurement. This scan geometry enables an isotropic voxel size of 0.4 mm^3.

The CT-CA protocols were performed after an intravenous administration of 100 ml of iodinated contrast agent (Iomeprol, Iomeron® 400 mgI/ml, Bracco, Milan) with an injection rate of 5 ml/s using an automatic power injector (Stellant, MedRAD, Pittsburgh, USA).

The synchronization between the CT scan and the arterial phase of contrast material was performed using the bolus-tracking technique (CARE bolus, Siemens, Forchheim, Germany). Image reconstruction was obtained using retrospectively ECG-gated reconstruction. The datasets were reconstructed at −300ms/−400ms before the next R-wave or at 60%/70% of the R-R interval (end-diastolic phase of the cardiac cycle).

The image reconstruction was performed with different temporal window, usually from 25% to 35% of R-R interval, when deemed necessary (i.e. motion-artefacts).

Quantitative Coronary Angiography (QCA)

I*CA* was performed within 2 weeks after non-invasive CA examination. One observer, blind to CT-CA results, performed the evaluation using a modified 17-segment AHA classification (19). All segments were included to evaluate CT-CA vs. ICA. Coronary artery segments were classified as normal (lumen and wall regular), non significant (irregular wall and lumen reduction <50%), significant (irregular wall and ³50% stenoses).

An orthogonal bi-dimension projection was used with a dedicated software (CAAS®, Pie Medical, Maastricht, NL) to quantify the degree of coronary stenosis (≥50% lumen reduction = significant).

CT-CA Image Analysis

Two observers blind to any other information about the patients evaluated all images. All segments were assessed for the presence of stenoses. The maximum-intensity and multiplanar projections were used to identify coronary plaques and non- or significant lesion (Figure 1 and 2).

Image quality was evaluated on a per-segment basis and classified as good (defined as the absence of any image-degrading artefacts related to motion or severe calcification), adequate (presence of image-degrading artefacts but evaluation possible with acceptable confidence) or poor (presence of image-degrading artefacts but evaluation possible with moderate confidence).

Data Analysis

Diagnostic performance of CT-CA in the detection of significant coronary artery stenosis was assessed using quantitative ICA as the gold standard CA, and expressed as sensitivity, specificity, positive and negative predictive value (95% confidence intervals). Inter- and intra-observer variability were calculated and expressed as percentage of agreement (κ). The statistical analysis was performed using a dedicated software (Statistical Package for the Social Sciences, versione 11.5, SPSS Inc., Chicago, Illinois).

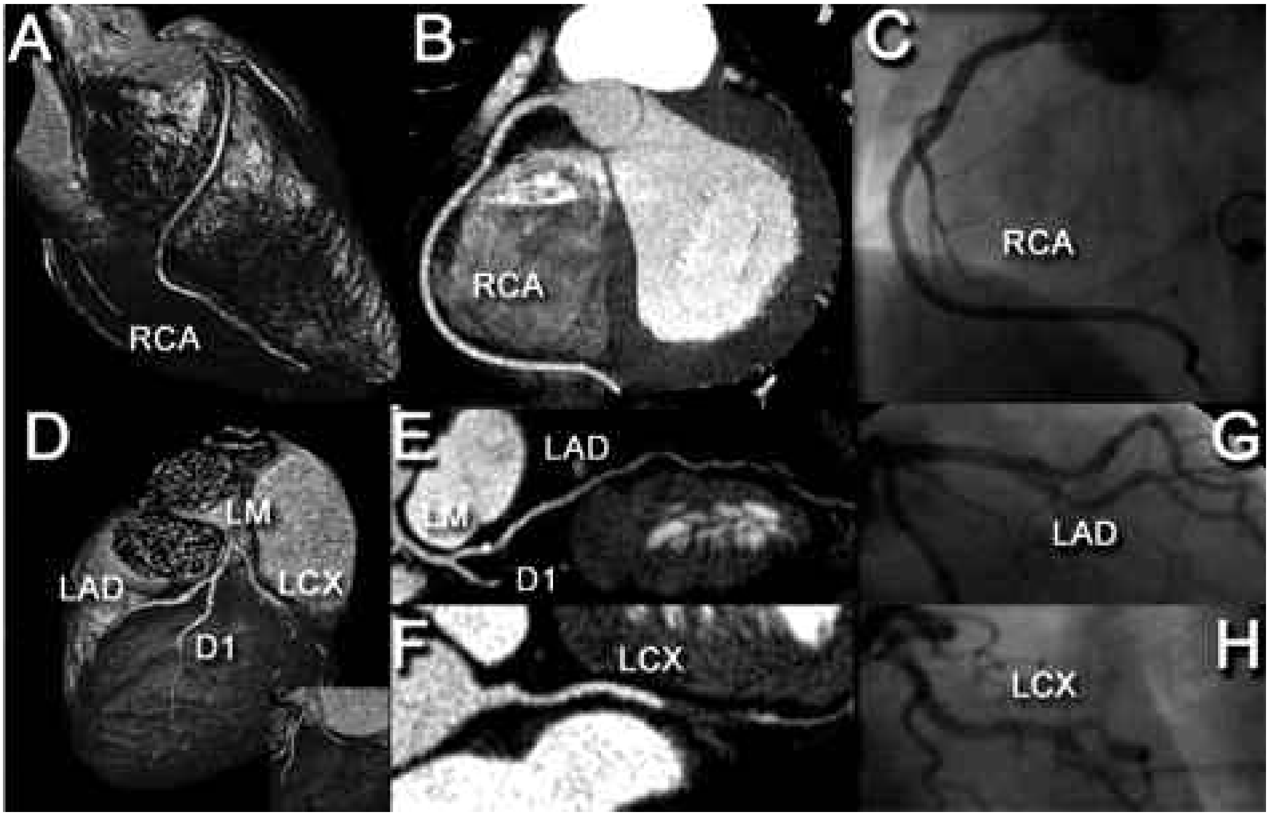

Figure 1. Left circumflex occlusion with 64-slice CT. The left coronary artery, without significant diseases and calcifications, appears to be patent (D, E). The correlation with conventional coronary angiography (G) is optimal. To be noticed the left circumflex coronary artery is occluded (D, F, H). The right coronary artery is patent and without lesion (A,B) with optimal correlation with conventional coronary angiography.
Abbreviations: LM = Left main; LAD = left anterior descending coronary artery; LCX = left circumflex coronary artery; RCA = right coronary artery; D1 = first diagonal branch

Results

In 73% (31/44) of the patient population we administered additional β-blockers and in 31% (13/44) we also administered lorazepam. The average scan time was 13.3±0.9s. Table 1 shows patient characteristics. Table 2 shows the distribution and extent of significant coronary artery disease as defined from ICA results (prevalence of disease 82%). None of the patients was excluded from the study population. Inter- and intra-observer variability, expressed as κ value, for the detection of significant coronary stenoses was 0.73 and 0.79, respectively. In 66% (29/44) of the patients, the data reconstruction was performed in the end-diastolic phase.

Image quality was classified as good in 93.4%, moderate in 4.7% and poor in 1.9% of coronary segments.

Poor image quality was due to image-degrading artefacts (50%, 6/12), severe calcifications (50%, 6/12) or low contrast/noise ratio (16.7%, 2/12).

Overall, 44 patients and 618 coronary segments were included in the study. Table 3 shows diagnostic accuracy of CT-CA for the detection of significant coronary artery stenoses. In the middle segment of coronary artery circumflex (LCX), a significant lesion (≥50% lumen reduction) was underestimated and classified as non significant by CT-CA (i.e. false negative); 25 non significant lesions were misdiagnosed and judged as significant by CT-CA (i.e. false positives).

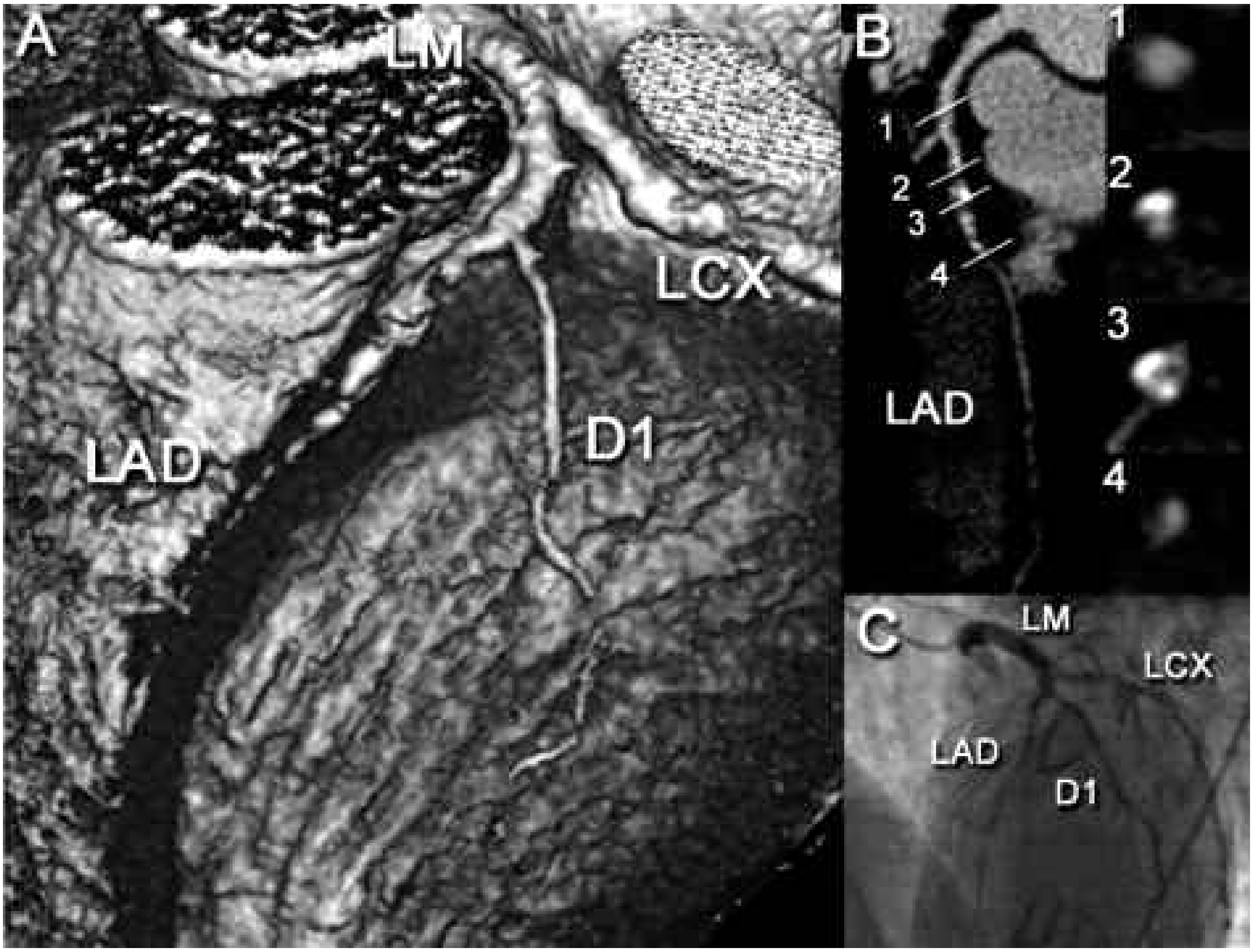

Figure 2. Coronary artery disease of the left anterior descending with 64-slice CT. A diffusely diseased left anterior descending coronary artery is displayed (A). In B the curved reconstruction shows the presence of large predominantly calcified plaques in the proximal left anterior descending coronary artery. In the distal part is occluded. The correlation with conventional coronary angiography is shown in C.
Abbreviations: LM = Left main; LCX = left circumflex coronary artery; D1 = first diagonal branch

Table 2. Distribution of Coronary Artery Disease

Absent or non significant disease (%)	8 (18.2)
Single-vessel disease (%)	12 (27.3)
Dual-vessel disease (%)	13 (29.5)
Triple-vessel disease (%)	11 (25)
Multi-vessel disease (%)	24 (54.5)
Total	44

Out of these lesions, 24% (6/25) were partially or completely calcified, and 12% (3/25) were in segments in which image quality was judged moderate (2/3) or poor (1/3) due to motion artefacts. Only one out of the 25 false positive lesions, instead, was in a segment judged of moderate quality due to poor contrast/noise.

Discussion

Several studies reported the earlier CT scanner generations as promising as non-invasive alternative to detect significant coronary artery stenosis (1-15). However, in these studies, the high values of diagnostic accuracy derived from assessable coronary artery segment (9, 10, 13, 14, 20-24).

Table 3. Diagnostic Accuracy of 64-slice CT-CA for ³50% coronary artery stenosis.

		N°	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value
Per-segment (total)		618	98.9%	95.2%	78.8%	99.8%
Per-vessel						
	RCA	44	100%	94.1%	96.4%	100%
	LM	44	100%	100%	100%	100%
	LAD	44	100%	73.7%	83.3%	100%
	LCX	43	94.4%	92.3%	89.5%	96.0%
Per-patient		44	100%	100%	100%	100%

Abbreviations: LM = Left Main; LAD = Left Anterior Descending; LCX: Left Circumflex; RCA = Right Coronary Artery

The latest 64-slice CT technology scanner offers an improved signal/noise ratio, better temporal and spatial resolution, and reduced scan time. CT-CA allows to investigate the entire coronary tree (proximal and distal vessels).

In our study CT-CA showed a sensitivity and a negative predictive value of 99% and 100%, respectively. This is in favour of a very useful imaging modality, in particular for the exclusion of disease. However, specificity and positive predictive values were 93% and 79%, respectively, reflecting a non negligible number of false positives. These values are reported on a per-segment basis. On a per-patient basis, the figures are slightly different.

All patients with negative ICA were correctly identified by CT-CA, suggesting again that CT-CA may be a useful tool for significant coronary artery disease exclusion. Only one >50% was underestimated as non significant with CT-CA. This appears only in the per-segment analysis since the patient had another significant lesion.

We must consider that our results were obtained in a highly selected patients' population with chest pain and a high prevalence of disease (82% on a per-patient basis) and in particular with a prevalence of multi-vessel disease of about 54%.

This high risk symptomatic patients population shows very high pre-test likelihood of disease. For this reason it is questionable to pose the indication for CT-CA even though the results are fairly good. On the other hand CT-CA may be a reliable alternative to ICA in situations in which Cath-lab and/or immediate revascularization is not possible/necessary.

Limitations

Estimated radiation dose was higher for CT-CA (15.2-21.4 mSv) as compared to ICA. At low heart rates, a dose reduction of up to 50% is possible appling prospective tube current modulation.

Conclusions

Non-invasive CT-A with 64-slice CT technology is a reliable alternative to ICA for the detection of significant coronary artery stenosis in a selected population of symptomatic patients with high risk of disease.

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