

Assessment of Coronary Plaques by 16-Row Multidetector Computed Tomography. Correlation with Intravascular Ultrasound

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ABSTRACT

Background

Atherosclerosis counts for 50% of cardiovascular deaths. Recent studies have demonstrated that certain atheromatous plaques with a lipid core and positive remodeling, known as vulnerable plaques, are more likely to develop plaque disruption, resulting in a coronary event. The early identification of these atheromatous plaques would have an extremely important clinical impact and might help to prevent the further development of an acute coronary syndrome.

Objective

To assess the diagnostic accuracy of coronary angiography with 16-row multidetector computed tomography (16-MCT) for the detection, characterization and quantification of atherosclerotic coronary artery lesions compared to intravascular ultrasound (IVUS).

Material and Methods

Forty five patients eligible to coronary angiography underwent 16-MCT and IVUS. Plaque burden and the characteristics of atheromatous plaques were analyzed in each coronary segment; plaques were classified in soft, fibrous and calcified. The binomial exact method was used to calculate the diagnostic accuracy of 16-MCT to determine the plaque burden and to identify coronary plaques. ROC curves analysis determined the cut-point for each type of plaque, as well as the mean density and the standard deviation expressed in Hounsfield units (HU). The diagnostic accuracy of the method for the diagnosis of coronary stenosis =50% was also assessed.

Results

The sensitivity and specificity of 16-MCT to detect plaque burden were 96.20% and 81.96%, respectively. For the detection of soft, fibrous and calcified plaques, the sensitivity and the specificity were 94.59% and 92.62%, 94.91% and 98.56%, and 93.22% and 95.13%, respectively. Using a cut-point of 85 HU, 16-MCT correctly identified 86% of soft and fibrous plaques, with an area under the ROC curve of 0.96; a cut-point of 196.68 HU resulted in an identification of 93% of calcified and non-calcified plaques, and the area under the ROC curve was 0.98. The sensitivity and specificity of the test for detecting coronary stenosis were 81.58% and 93.86%, respectively.

Conclusion

16-MCT is a promising non-invasive diagnostic tool for the assessment of patients with coronary artery disease, useful for the detection and characterization of the different types of plaques.

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Key words > Tomography - X-Ray Computed - Coronary Artery Disease

Abbreviations >	16-MCTCA 16-row multidetector computed tomography coronary angiography	IVUS Intravascular ultrasound
	CA Coronary angiography	ACSs Acute coronary syndromes
		HU Hounsfield units

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BACKGROUND

Acute coronary syndromes (ACSs) are one of the main causes of morbidity and mortality in the Western world; (1) 50% of deaths related to cardiovascular diseases are due to atherosclerotic disease and half of them are sudden and unexpected deaths. Acute coronary syndromes result from two principal physiopathological processes: plaque rupture and subsequent thrombosis (2). In addition, it should be noted that patients with ACSs present a high risk of a new coronary event within the first year of the acute episode.

Recent studies have demonstrated that certain atheromatous plaques with a lipid core and positive remodeling, known as vulnerable plaques, are more likely to produce a coronary event. (3) The early identification of these atheromatous plaques would have an extremely important clinical impact and might help to prevent the further development of an ACS.

Intravascular ultrasound (IVUS) is the method of reference which enables the in vivo assessment of the size, composition and morphology of atherosclerotic plaques and the complete visualization of the circumference of the coronary artery wall and vascular lumen. (4-6) Nevertheless, we should not forget that IVUS is an invasive and expensive procedure; morbidity and mortality rates related to IVUS are low, though real. These disadvantages limit its use in most patients submitted to coronary angiography (CA). For this reason it is necessary to find an alternative non-invasive diagnostic tool that will provide information similar to IVUS but with lower risk. This method should be effective in the detection and characterization of atherosclerotic disease in moderate to high-risk patients. (7-11)

The goal of the present study is to assess the diagnostic accuracy of coronary angiography with 16-row multidetector computed tomography (16-MCT) for the detection, characterization and quantification of atherosclerotic coronary artery lesions compared to IVUS.

MATERIAL AND METHODS

Patients

An independent Committee on Ethics approved the study protocol and all the patients signed an informed consent form before being included.

Between March and December 2005, 45 consecutive patients (40 men; mean age 60 years) eligible to coronary angiography were studied. Patients with unstable angina, atrial fibrillation, renal dysfunction (serum creatinine > 1.5 mg/ml) or with contraindications for the use of iodinated contrast agents were excluded from the study.

MCTCA Protocol

MCTCA was performed with a 16-row multidetector computed tomography scanner (Brilliance 16; Philips Medical Systems, Cleveland, OH). Scan parameters were as follows: slice collimation 16×0.75 mm, slice thickness 0.8 mm, reconstruction interval 0.4 mm, gantry rotation time 0.4 seconds; 140 kV; 500 mA. Patients received a mean radiation

dose of 10 mSv (± 2.5 mSv) and the scan time varied from 20 to 26 seconds depending on the length of the area being imaged.

Patients with a heart rate > 60 bpm were treated with oral atenolol at a dose of 25 -100 mg, 48 to 72 hours before the scan depending on basal heart rate values. In cases of high heart rate before the study, intravenous propranolol (40-80 mg) was administered in the scan room. A total of 100 ml of iodinated contrast agent (350 mg/ml, meglumine ioxitalamate; Telebrix C, Temis-Lastalo Laboratories, Argentina) was administered using a power injector with a dual-phase injection technique (60 ml at 4 ml/sec and 40 ml at 2.5 ml/sec). Image acquisition was performed in supine position while the patient held breath. The scan automatically started when the peak contrast enhancement reached the level of the aortic root in order to achieve an adequate opacification of the coronary tree (Bolus Pro Ultra; Philips Medical Systems, Cleveland, Ohio).

IVUS Protocol

Coronary angiography and IVUS were performed within the 7 days of the MCTCA. All patients received aspirin (100-325 mg/day) 72 hours before the study, and unfractionated heparin (70 UI/kg) and 0,2 mg of nitroglycerin were administered through an arterial line immediately before the CA. The procedure was performed under fluoroscopic guidance using the transfemoral Judkins technique. IVUS was carried out with a 3.2-Fr, 30-MHz coronary catheter with a resolution of 0.07/0.20 mm. The catheter was advanced as distally as the diameter of the vessel admitted. Continuous images were recorded as the catheter was automatically pulled back at a speed of 0.5 mm/sec. Once the study ended, an additional dose of 0.2 mg of nitroglycerine was administered in the coronary arteries to avoid coronary spasm.

Images Analysis

Images obtained with IVUS and MCTCA were analyzed by two independent observers.

MCTCA images were sent to a workstation (Extended Brilliance Workstation; Philips Medical Systems, Highland Heights, OH) and processed; images orthogonal to the axis of the studied vessel were divided in 10-mm segments until a luminal diameter = 1.5 mm was reached. The phase with the fewest motion artifacts was used for analysis; images were classified in three groups, according to their quality:

Group 1: high-quality images; absence or motion artifacts. The vessel can be correctly assessed.

Group 2: moderate-quality images; the vessel may be evaluated in presence of minimal motion artifacts.

Group 3: low-quality images; the vessel cannot be assessed due to the presence of motion artifacts.

IVUS images were analyzed with a special program (DigiView, Meditech S.A., Buenos Aires, Argentina). Images orthogonal to the axis of the vessel were generated at 10-mm increments from the coronary ostia to the most distal segments with a diameter = 1.5 mm.

Cross-sectional images from both methods were matched and the following determinations were performed in each segment:

- 1) Coronary plaque burden (PB), using the formula: $[1 - (\text{area of the lumen}/\text{area of the vessel})] \times 100$. A value = 50% was considered PB.
- 2) Plaque characterization. Coronary plaques were classified in three types in both studies:
 - a) Soft plaques:
 - IVUS: > 80% of the plaque area was composed of tissue with lower echogenicity compared to the vessel adventitia, without acoustic shadows.

- **MCTCA:** the density of the coronary plaque was lower than the tissue proximal to the vascular wall and than the vascular lumen, visible in at least two different planes.
- b) **Fibrous/intermediate plaques:**
 - **IVUS:** > 80% of the plaque was composed of tissue with greater echogenicity than the adventitia, without acoustic shadows.
 - **MCTCA:** the density of the coronary plaque was lower than the area of the lumen but greater than soft plaques, visible in at least two different planes.
- c) **Calcified plaques:**
 - **IVUS:** > 80% of the plaque was composed of tissue with greater echogenicity than the adventitia, with evidence of acoustic shadows.
 - **MCTCA:** the density of the coronary plaque was greater than the area of the lumen (in plaques proximal to the vessel) or with a density greater than 150 UH if visualized separated from the lumen, visible in at least two different planes.

The coronary tree was divided in 16 segments in order to grade coronary artery stenosis according to the classification of the American Heart Association. (12) A diameter reduction = 50% was considered a positive finding and defined significant stenosis.

Multiplanar reconstruction curves along the lumen of the coronary arteries, cross-sectional images (orthogonal to the axis of the vessel) and maximum intensity projections were used to analyze MCTCA.

Coronary angiographies were assessed by an independent observer and the outcomes were considered a reference for the analysis.

Statistical Analysis

The estimation of plaque burden, the characterization of coronary plaques and the severity of coronary artery stenosis were assessed with the binomial exact method, with determinations of sensitivity, specificity, positive predictive value and negative predictive value, with their corresponding 95% confidence intervals. At a second analysis, soft plaques and fibrous plaques were included in a same group under the denomination of "non-calcified plaques". The tomographic density was calculated in Hounsfield units (HU) and ROC curves were analyzed to establish cut-points among the different types of plaques.

RESULTS

The final analysis included 43/45 patients (95.5%). All patients had low heart rate during the image acquisition (mean: 55 beats per minute range: 44-61); thus, motion artifacts were absent. Two patients who were unable to hold breath during the acquisition and presented motion artifacts were excluded from the analysis. Patients with coronary artery bifurcation lesions were not excluded; no complications related to IVUS or to the injection of contrast media agents were reported.

Plaques characterization

One hundred and ninety six segments in 43 coronary arteries were assessed (left anterior descending coronary artery n = 24; circumflex coronary artery n = 13 and right coronary artery n = 6). The quality of

the images was grade 1 in 111 segments and grade 2 in 85 segments. No segments with a quality of image grade 3 were observed.

Figure 1 and figure 2 show the quantification of plaque burden. IVUS determined 76 coronary segments with PB = 50%, while MCTCA detected 88 segments (Table 1). IVUS identified 196 plaques in 196 segments and MCTCA identified 202 plaques. Table 2 describes the statistical results according to the types of plaques; soft plaques and fibrous plaques are included in a sub-group as non-calcified plaques. Mean density of plaques was 43.04 ± 36.14 HU for soft plaques, 128.12 ± 35.02 HU for fibrous plaques and 370.20 ± 201.45 HU for calcified plaques.

Using a cut-point of 85 HU, 16-MCT correctly identified 86% of soft and fibrous plaques, with an area under the ROC curve of 0.96 (95% CI: 0.93-0.98) (Figure 3) A cut-point of 196.68 UH resulted in an identification of 93% of calcified and non-calcified plaques, and the area under the ROC curve was 0.98 (95% CI: 0.96 to 1) (Figure 4).

Quantification of Coronary Stenosis

We assessed 668/688 coronary segments with a diameter = 1.5 mm. Twenty segments (3%) with a diameter < 1.5 mm were not evaluated and were excluded from the analysis. The statistical results of the diagnostic accuracy of MCTCA for the detection of coronary artery stenosis = 50% are described in Table 3.

DISCUSSION

The results of this study suggest that MCTCA is a useful tool for the detection and characterization of coronary plaques. Achenbach et al (13) had previously assessed the potential role of MCTCA in the characterization of coronary artery disease compared with IVUS in 22 patients, and reported a sensitivity of 94% for identifying calcified plaques. This finding is similar to our sensitivity of 93.2%. (14) Nevertheless, they reported a lower sensitivity to detect soft plaques; however, the low prevalence of soft plaques in their population compared to ours (30% versus 56%, respectively) may account for this difference.

Leber et al (15) correlated the findings of 64-row detector MCTCA with IVUS and informed an excellent diagnostic accuracy and correlation in the assessment of the area of the lumen and the characterization of coronary plaques. Nevertheless, they informed the limitations of MCTCA for the quantification of the severity of lesions, which may be probably due to a suboptimal positive predictive value of the method, especially related with the presence of calcified plaques and motion artifacts.

The density of soft plaques and fibrous plaques informed by Schoreder et al. (16) in HU is lower compared to our results; perhaps this difference may be due to the lower number of lesions evaluated in their study.

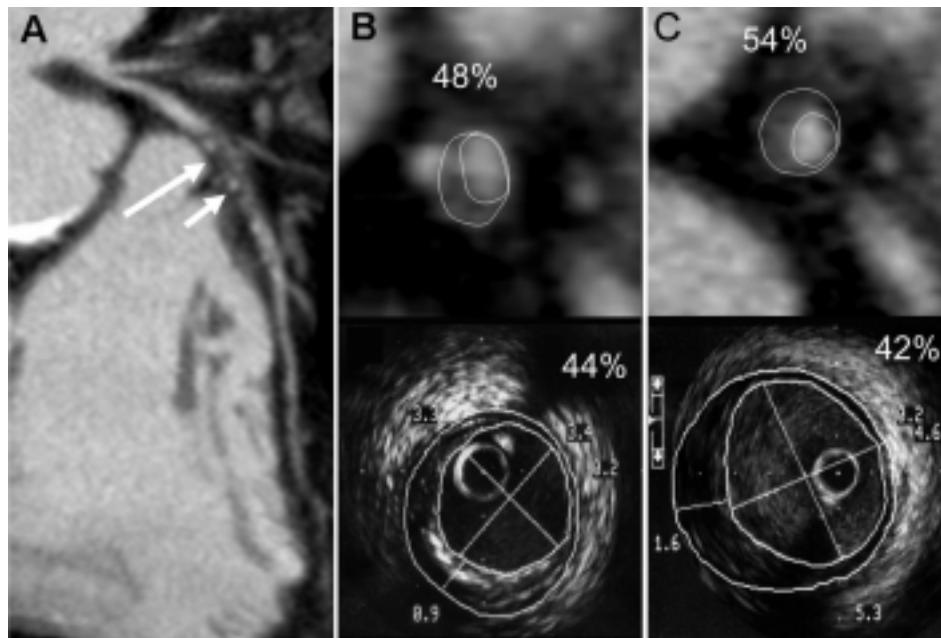


Fig. 1. A 61-year old male patient with a history of hypertension and dyslipemia. **A.** Multiplanar reconstruction curve of the left anterior descending coronary artery showing a soft plaque in the mid-artery segment with positive remodeling and reduction in the lumen of the artery. The arrows show the level of the segments assessed by MCTCA and IVUS in **B** (*big arrow*) and **C** (*small arrow*) **B** and **C.** Axial MCTCA images, orthogonal to the axis of the vessel (above) and IVUS images (below) of the same coronary artery segment, showing the presence of atherosclerotic disease and the percentage of plaque burden in each level.

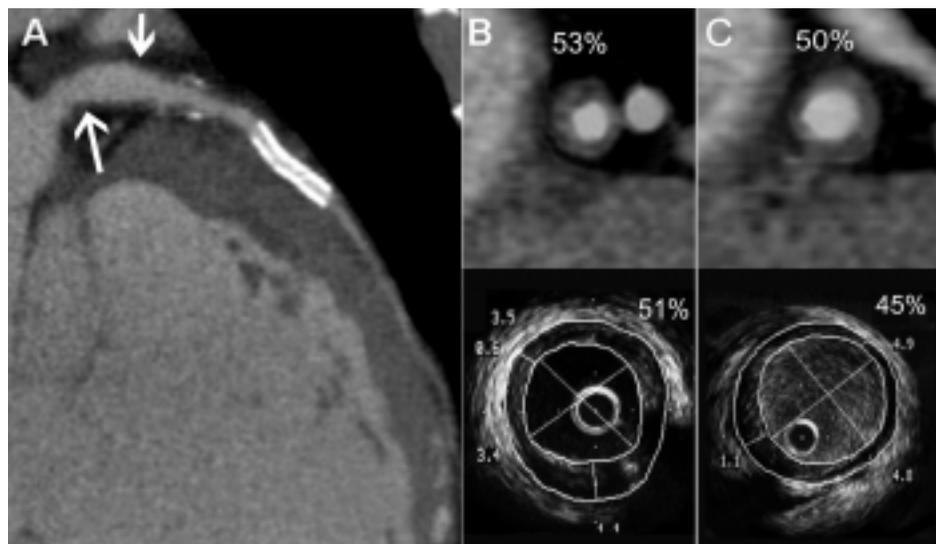


Fig. 2. A 58-year old male patient with a history of angioplasty to the left anterior descending coronary artery. **A.** Multiplanar reconstruction curve of the left anterior descending artery showing atherosclerotic disease in the proximal-artery segment with positive remodeling and slight lumen reduction. The arrows show the level of the segments assessed by MCTCA and IVUS in **B** (*big arrow*) and **C** (*small arrow*) **B** and **C.** Axial MCTCA images, orthogonal to the axis of the vessel (above) and IVUS images (below) of the same coronary artery segment, showing the presence of atherosclerotic disease and the percentage of plaque burden in each level.

In our first experience with a 4-row detector computed tomography scanner in 40 patients, our results were similar to those of the current study; nevertheless, it should be mentioned that the 16-row detector scanner is able to assess coronary segments with a diameter of 1.5mm instead of 2 mm. (14) MCTCA allows a correct differentiation of fibrous plaques, with a cut-point of 79 HU established by the ROC curves. This means that the method has an excellent power to discriminate between calcified and non-calcified plaques with a cut-point of 199 HU, a value similar to the finding in our initial experience (180 HU). Mean density of soft, fibrous and calcified plaques was 43.04 ± 36.14 , 128.12 ± 35.02 y 370.20

± 201.45 HU, respectively, and these densitometric values are similar to those we have previously reported.

Recent studies carried out in patients with acute coronary syndromes have demonstrated that plaques responsible for the coronary event have certain characteristics of vulnerability related to their composition (a lipid core with tiny foci of calcification scattered throughout the plaque) and to the degree of remodeling. (3) There is no data available yet on the prognostic value of these types of plaques in patients who have not suffered an acute coronary event. Further multicenter trials and retrospective studies will be necessary to determine this issue.

MCTCA might be useful to characterize obstructive plaques and therefore guide the selection of a percutaneous coronary intervention and/or the most adequate device; for example, direct stenting for soft plaques versus atherectomy for fibrous and calcified plaques.

This study was performed with a 16-row multidetector computed tomography scan; thus as technology progresses, an increase in the number of detectors might enable us to achieve better temporal and spatial resolution enhancement, giving more details of the vascular wall and the possibility of analyzing vessels with smaller diameters. Another limitation of the procedure that is also seen with invasive angiography is related to the use of iodinated contrast agents in patients with renal failure or with a history of adverse reactions to these agents.

Table 1. Quantification of coronary plaque burden. Diagnostic accuracy

	MCTCA
TP	76
TN	50
FP	11
FN	3
Sensitivity	96.20% (CI 91.92%-100%)
Specificity	81.96% (CI 72.31%-91.61%)
Positivity predictive value	97.35% (CI 80.37%-94.33%)
Negative predictive value	94.33% (CI 88.11%-100%)

MCTCA: Multislice computed tomography coronary angiography TP: True positives. TN: True negatives. FP: False positives. FN: False negatives. CI: 95% confidence interval.

Table 2. Detection of coronary plaques with multidetector computed tomography scanner

	Soft plaques	Fibrous plaques	Non-calcified plaques	Calcified plaques
TP	70	56	126	55
TN	113	137	250	313
FP	9	2	11	16
FN	4	3	7	4
S	94.59% (CI 89.44%-99.74%)	94.91% (CI 89.30%-100%)	94.73% (CI 90.94%-98.53%)	93.22% (CI 86.80%-99.63%)
E	92.62% (CI 87.98%-97.26%)	98.56% (CI 96.58%-100%)	95.78% (CI 93.34%-98.22%)	95.13% (CI 82.81%-97.46%)
SP	88.60% (CI 81.60%-99.61%)	96.55% (CI 91.85%-100%)	91.97% (CI 87.42%-96.52%)	77.46% (CI 67.74%-87.18%)
VPP	96.58% (CI 93.28%-98.87%)	97.85% (CI 95.45%-100%)	97.27% (CI 95.28%-99.26%)	98.73% (CI 97.50%-99.96%)

TP: True positives. TN: True negatives. FP: False positives. FN: False negatives. S: Sensitivity SP: Specificity VPP: Positive predictive value NPV: Negative predictive value CI: 95% confidence interval.

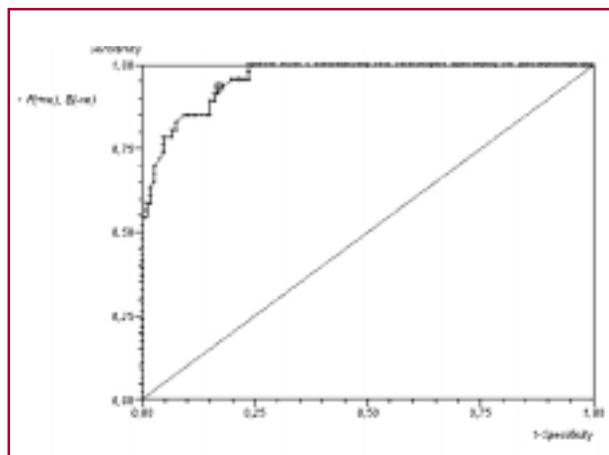


Fig. 3. ROC curve with a cut-point of 85 HU between soft plaques and fibrous plaques with an area under the curve = 0.96 (95% CI: 0.933-0.98) for a sensitivity of 93% and a specificity of 83%.

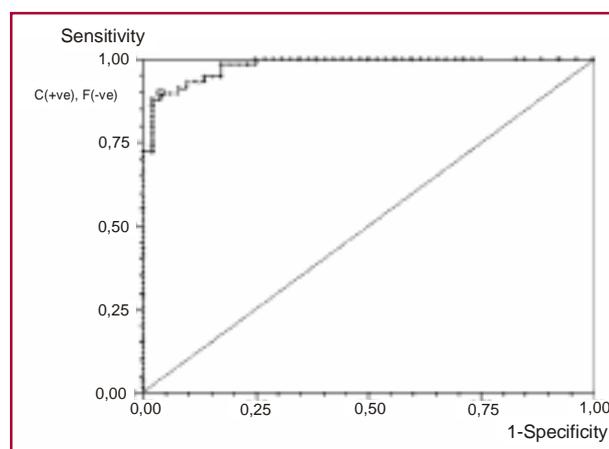


Fig. 4. ROC curve with a cut-point of 196.68 HU between calcified plaques and non-calcified plaques with an area under the curve = 0.98 (95% CI: 0.933-0.98) for a sensitivity of 90% and a specificity of 96%.

Table 3. Diagnostic accuracy of MCTCA for the detection of coronary artery stenosis = 50%

	ACTCM
TP	93
TN	520
FP	34
FN	21
Sensitivity	81.58% (CI 73.23%-88.22%)
Specificity	93.86% (CI 91.53%-95.71%)
Positive predictive value	73.23% (CI 63.65%-80.69%)
Negative predictive value	96.12% (CI 94.13%-97.58%)

MCTCA: Multislice computed tomography coronary angiography TP: True positives. TN: True negatives. FP: False positives. FN: False negatives. CI: 95% confidence interval.

CONCLUSION

MCTCA is a promising non-invasive diagnostic tool for the assessment of patients with coronary artery disease, useful not only for evaluating the vascular lumen and the arterial wall, but also for the detection and characterization of the different types of plaques. Compared to IVUS, MCTCA can be performed in greater number patients. The development of new scanners with more detectors and better temporal and spatial resolution encourages us to think that MCTCA will turn out to be not only an invaluable diagnostic tool but also useful to determine the prognosis of coronary artery disease, as well as the response to coronary atherosclerotic plaque in a large population of patients under hypolipidemic therapy.

RESUMEN

Introducción

El 50% de las muertes de etiología cardiovascular se deben a la enfermedad arteriosclerótica. Estudios recientes demostraron que las placas ateromatosas más propensas al desarrollo de un evento coronario son las que presentan ciertas características particulares, como un centro o *core* lipídico y remodelación positiva, denominadas placas vulnerables. La determinación temprana de la presencia de este tipo de placas aterioscleróticas tendría un impacto clínico de suma importancia y podría ayudar a prevenir el desarrollo de un síndrome coronario agudo en el futuro.

Objetivo

Determinar la certeza diagnóstica de la angiografía coronaria por tomografía computarizada multidetector de 16 filas (16-ACTCM) en la identificación, la caracterización y la cuantificación de las lesiones arterioscleróticas coronarias en comparación con la ecografía intravascular (EIV).

Material y métodos

Se estudiaron 45 pacientes con indicación de angiografía coronaria con 16-ACTCM y EIV. En cada segmento coronario

se analizaron la carga de placa y las características de la placa aterosclerótica, que se clasificó en blanda, fibrosa y cálcica. La certeza diagnóstica de la 16-ACTCM para determinar la carga de placa y la identificación de placas coronarias se calculó con el método exacto binomial. Sobre la base de un análisis con curvas ROC se determinó el punto de corte para cada tipo de placa, así como la densidad media y la desviación estándar en unidades Hounsfield [UH]). Se evaluó además la certeza diagnóstica de la ACTCM para el diagnóstico de estenosis coronaria $\geq 50\%$.

Resultados

Para la detección de carga de placa, la sensibilidad fue del 96,2% y la especificidad fue del 81,9%. Para la detección de placas blandas, fibrosas y calcificadas, la sensibilidad y la especificidad fueron del 94,6% y 92,62%, del 94,9% y 98,5% y del 93,2% y 95,1%, respectivamente. Con un valor de corte de 85 UH, la 16-ACTCM diferenció correctamente el 86% de las placas blandas y fibrosas, con un área ROC = 0,96; con un valor de corte de 196,7 UH diferenció correctamente el 93% de las placas calcificadas y no calcificadas, con un área ROC = 0,98. Para la detección de estenosis coronaria, la sensibilidad fue del 81,58% y la especificidad fue del 93,8%.

Conclusión

La 16-ACTCM es una modalidad diagnóstica no invasiva promisoría para el estudio de pacientes con enfermedad coronaria, ya que permite la detección y la caracterización de los diferentes tipos de placa.

Palabras clave > Tomografía computarizada por rayos X - Coronariopatía

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Competing interests

None declared.