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Should computed tomography coronary angiography be aborted when the calcium score exceeds a certain threshold in patients with chest pain?

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ABSTRACT

Background: There is ongoing debate about whether a computed tomography coronary angiography (CTCA) should be aborted when the calcium score (CS) exceeds a certain threshold in patients with chest pain. The aim of this study was to discover whether specific "cutpoints" regarding coronary artery CS could be determined to predict severe coronary stenoses assessed by CTCA, thus identifying patients amenable to an invasive diagnostic approach.
Methods: 294 consecutive patients with chest pain of uncertain cause who were referred for non-invasive diagnostic CTCA were included. Subjects underwent Agatston CS and CTCA using current 64-slice technology.
Results: Severe coronary stenoses were noted in 75 of 294 (25.1%) patients on CTCA. A very high prevalence of severe coronary stenoses was found in patients with CS ≥400 (87.0%). The CS had area under the ROC curve 0.86 to predict severe coronary stenoses on CTCA. The best discriminant cut-off point was CS ≥400 (sensitivity of 55.3%, specificity of 93.5, positive predictive value of 85.8%, negative predictive value of 84.0%). Multivariable logistic regression analysis controlling for traditional risk factors showed CS ≥400 remained an independent predictor of severe coronary stenoses on CTCA (OR 14.553, 95% confidence interval 4.043 to 52.384, $p<0.001$).
Conclusions: CS can be used as a "gatekeeper" to CTCA in patients with chest pain. Due to the very high prevalence of severe coronary stenoses in patients with CS ≥400, further evaluation with CTCA is not warranted as these patients should be referred to invasive coronary angiography, avoiding the repeated exposure to ionizing radiation and iodinated contrast.

1. Introduction

Coronary artery calcium is closely correlated with atherosclerotic plaque formation and thus is a sensitive marker of existing atherosclerosis [1–4]. Coronary calcium score (CS) using computed tomography has been validated as a tool for optimizing risk stratification regarding the development of non-fatal and fatal cardiac events [5–9]. Recently, multidetector computed tomography (MDCT) has emerged as a non-invasive technique that facilitates reliable detection of coronary artery stenoses. However, it remains controversial whether to proceed with a computed tomography coronary angiography (CTCA) in the presence of extensive coronary calcification. Calcified plaques produce artifacts (blooming) which may affect the evaluation of luminal obstruction [10–12]. At the same time, more extensive coronary calcification increases the likelihood that the patient has obstructive coronary artery disease [13], and invasive coronary angiography is required in most cases for the definite diagnosis and treatment. This has led to an ongoing debate as to whether a CTCA should be aborted in symptomatic patients when the CS exceeds a certain threshold, avoiding the repeated exposure to ionizing radiation and iodinated contrast. A generally accepted cut-off value is lacking, and proposed thresholds are arbitrarily chosen. The aim of the present study was to discover whether specific ranges of values, or "cutpoints," regarding coronary artery CS could be determined to predict the presence of severe coronary stenoses assessed by CTCA in patients with chest pain, thus identifying those amenable to direct invasive diagnostic approach. We also evaluated the value of CS beyond traditional cardiovascular risk factors for predicting CTCA obstructive lesions.

2. Methods

2.1. Study population

From January 2007 to December 2010, 294 consecutive patients with chest pain of uncertain cause who were referred for non-invasive diagnostic CTCA were included. Demographic and clinical characteristics, including age, sex, cardiovascular risk factors

Abbreviations: CS, calcium score; CTCA, computed tomography coronary angiography; ECG, electrocardiogram; MDCT, multidetector computed tomography; ROC, receiver operating characteristic.

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(hypertension, diabetes mellitus, hyperlipidemia, smoking status), kidney failure and peripheral arterial disease were identified. Kidney failure was defined as a serum creatinine level of more than 1.3 mg/dl (115 μmol/l). Patients with atrial fibrillation, significant renal insufficiency, or history of significant iodinated contrast allergy were excluded. In addition, we excluded those with a previously documented history of obstructive coronary artery disease. All patients gave written informed consent for MDCT in accordance with a protocol approved by the institutional review board. The decision whether to perform invasive coronary angiography was taken by the patient's physician in all cases based on age, risk level and severity or persistence of symptoms. The authors of this manuscript have certified that they comply with the Principles of Ethical Publishing in the International Journal of Cardiology.

2.2. MDCT acquisitions

MDCT data were acquired using Brilliance 64 MDCT (Philips Medical Systems, Best, the Netherlands). Before CS and CTCA examinations, heart rate and blood pressure were monitored. In the absence of contraindications, subjects received propranolol (5–15 mg intravenously) if the resting heart rate exceeded 65 bpm. All subjects were in sinus rhythm. The heart rate of all subjects ranged between 49 and 75 bpm (average, 64 ± 3 bpm) with or without premedication. The subjects were imaged in the supine position. The subjects were instructed to maintain an inspiratory breath-hold during which the MDCT data and ECG trace were acquired. Scanning was performed from the tracheal bifurcation to 1 cm below the diaphragmatic face of the heart. First, a native retrospectively electrocardiographic (ECG)-gated scan without contrast media was performed to determine the CS. After a scout scan a volume of 80 to 120 ml of contrast media (iopamidol 370 mg I/ml, Bracco) was injected intravenously via an 18-gauge catheter placed in the antecubital vein, at a rate of 5 ml/s and controlled with a bolus-tracking technique, followed by a bolus of 50 ml of saline. Scanning started automatically with a delay of 5 s after a predefined threshold of 140 HU was reached in the aortic root. Scanning was performed at 120 kV, with an effective tube current of 600 to 1000 mAs, slice collimation of 64×0.625-mm acquisition, gantry rotation time of 0.4 s, and pitch of 0.2. Image reconstruction was done routinely using the retrospective ECG-gating method. The effective dose of the nonenhanced scan and the CTCA was estimated from the dose–length product and an organ weighing factor [$k = 0.014\ mSv \times (mGy \times cm)^{-1}$] for the chest as the investigated anatomical region [14].

2.3. Image processing and analysis

Post-processing of the CS and CTCA examinations were performed on dedicated workstations (Philips Extended Brilliance Workspace). For each study, a CS was determined using the methods of Agatston et al. [15]. Coronary CS was measured without contrast using semiautomatic software (HeartBeat CS, Philips Medical Systems) that displayed colored spots for calcium to be manually marked by the operator and automatically calculated all spots to a summed CS (Fig. 1). A CS was calculated for each epicardial coronary segment and recorded as a composite (i.e., total or summed) score for the entire epicardial coronary system (left main, left anterior descending, left circumflex and right coronary arteries). The total CS was used to divide patients into 7 groups: 0–100, 101–200, 201–300, 301–400, 401–600, 601–800, and >800. Contrast-enhanced multidetector computed tomograms were examined for presence of obstructive coronary luminal narrowing in all available segments. CTCA angiograms were examined using the axial slices, curved multiplanar reconstructions, and maximum intensity projections (Fig. 1). Coronary arteries were divided into 17 segments based on the recommendations of the modified American Heart Association [16]. Each vessel was analyzed on at least two planes, one parallel, and one perpendicular to the course of the vessel. Semiquantitative assessment was performed on all segments of the coronary artery tree, with an estimate of stenosis severity calculated as the ratio of the minimum contrast lumen over the normal reference lumen of an unaffected distal portion. Severe coronary stenosis was defined as greater than 70% reduction of the lumen diameter. Scans were analyzed by a consensus of an experienced radiologist and a cardiologist, who were both blinded to the clinical history. Discrepancies were resolved after additional joint review and discussion. For the pattern of calcium deposit assessment in each lesion a 10 mm long segment of artery centered on the minimum lumen site was analyzed and categorized into 1 of 4 groups: (1) no calcification: a lesion in which calcium was not detected; (2) spotty calcification: a lesion that contained only small calcium deposits within an arc of less than 90°; (3) intermediate calcification: a moderate calcific lesion with an arc of 90° to 180° in >1 cross-sectional image of the lesion; and (4) extensive calcification: an extensive calcific lesion with an arc of more than 180° in >1 cross-sectional image of the lesion. Image quality was classified for each segment as being excellent (no artifacts, unrestricted evaluation), adequate (minor artifacts, good diagnostic quality), and poor/not evaluative (severe artifacts impairing accurate evaluation). For the analysis the study population was divided into two groups: group 1 ($n = 219$): no severe coronary stenoses on CTCA, and group 2 ($n = 75$): severe coronary stenoses on CTCA.

2.4. Statistical analysis

Continuous variables are presented as mean ± SD. Categorical data are presented with absolute frequencies and percentages. Differences between groups for continuous variables were analyzed using Student's t-test (when group distributions were symmetrical and mounded) or Mann–Whitney U test (when group distributions were skewed). Chi-square test (when all expected cell counts were >5) or Fisher's exact test (when any expected cell count was <5) was used to determine the significance of differences in categorical variables. Uni and multivariate logistic regression analysis was used to analyze predictors of severe coronary stenoses on CTCA. Receiver operating characteristic (ROC) curves were plotted to determine the optimal cut-off values for CS prediction of severe coronary stenoses on CTCA. Two-tailed $p < 0.05$ was considered statistically significant. All statistical analyses were performed using SPSS version 15.0 (SPSS Inc, Chicago, IL, USA).

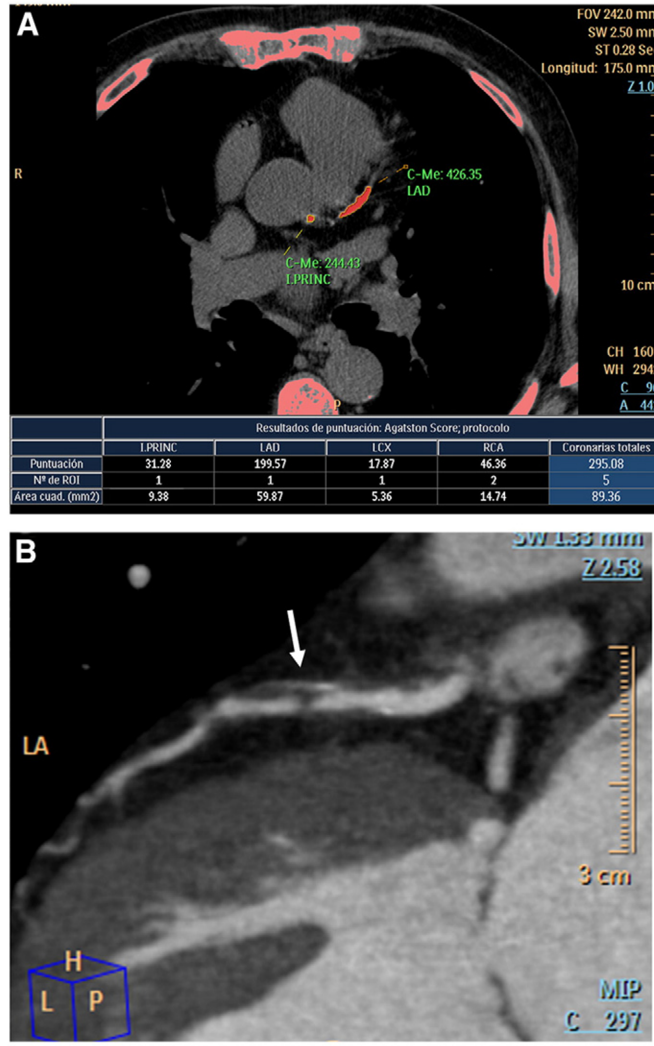

Fig. 1. Multidetector computed tomogram findings in a 56-year-old man with chest pain of uncertain cause. The coronary calcium score was 295 (panel A). Contrast-enhanced MDCT showed a severe luminal stenosis in the proximal left anterior descending coronary artery (panel B, arrow).

3. Results

3.1. Patient data

Mean age was 64.28 ± 12.3 years and 45.9% was male. All MDCT examinations were performed without complications. The estimated average effective radiation exposure was 1.5 ± 0.4 mSv for CS and 13.2 ± 5.3 mSv for CTCA. Image quality was rated as being excellent in 64% (3199/4998), adequate in 33% (1649/4998), and poor in 3% (150/4998), of all segments. Of the 3% that were not assessable, 90 (1.8%) were affected by heavy calcification, and 60 (1.2%) because of a lack of image quality such as coronary motion, vessel size, breathing artifacts, or technical scan insufficiencies such as scan abortion, misplaced scan range, poorly executed contrast media timing, or ECG misregistrations. The most frequently non assessable segment was