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Multi-slice computed tomography: Can it adequately rule out left main coronary disease in patients with an intermediate probability of coronary artery disease?

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Abstract

Background: *Multi-slice computed tomography (MSCT) is a fast-growing technology that permits a non-invasive, yet reliable, assessment of coronary atherosclerosis. We sought to explore the diagnostic accuracy of MSCT angiography in the detection of significant stenosis of the left main coronary artery (LMCA) in a series of patients with an intermediate pre-test likelihood of coronary artery disease (CAD).*

Methods: *We prospectively enrolled 30 consecutive patients with an intermediate pre-test likelihood of CAD. Patients underwent 64-slice MSCT angiography to detect significant stenosis of the LMCA (defined as ≥ 50% luminal obstruction). They subsequently underwent invasive coronary angiography according to the standard technique.*

Results: *The mean age was 52.7 ± 6.3 years, 24 (80%) being males. Three (10%) patients had significant stenosis of the LMCA by invasive coronary angiography, while four (13.3%) patients were categorized as having significant LMCA stenosis by MSCT coronary angiography. MSCT coronary angiography was able to detect significant LMCA stenosis with a sensitivity of 100%, specificity of 96.3%, positive and negative predictive values of 75% and 100% respectively, and a diagnostic accuracy of 96.7%, with reference to invasive coronary angiography.*

Conclusions: *In patients with an intermediate pre-test likelihood of CAD, MSCT coronary angiography provides a highly accurate diagnostic modality for ruling out significant LMCA stenosis, with reference to invasive coronary angiography.* (Cardiol J 2010; 17, 6: 594–598)

Key words: multi-slice computed tomography, coronary angiography, left main coronary artery

Introduction

Multi-slice computed tomography (MSCT) is a rapidly advancing technology that permits a non-invasive, yet reliable, assessment of coronary atherosclerotic disease. An accumulating body of evidence has demonstrated a consistently high sensitivity and specificity for the detection of significant coronary stenosis, as compared to standard invasive coronary angiography [1–4]. Yet, based on its high negative predictive value, it has become an accepted diagnostic option to exclude coronary artery disease (CAD) in patients with chronic stable angina pectoris; a normal MSCT scan almost rules out sig-

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nificant coronary stenosis [5, 6]. Furthermore, a normal MSCT foretells a good prognosis at mid-term follow-up, which compares favorably with that of a normal coronary angiogram [7].

The prevalence of a normal MSCT in a population with suspected CAD depends on the pre-test likelihood of the disease. The yield of a normal scan was highest in patients with low or intermediate pre-test likelihood of coronary disease [8]. In a population with a Bayesian distribution, MSCT angiography (being a non-invasive test) is expected to have the greatest impact on supporting or ruling out the diagnosis of significant CAD in subjects with an intermediate pre-test likelihood of the disease.

In a prospective study design, we sought to explore the diagnostic accuracy of MSCT angiography for the detection of significant stenosis of the left main coronary artery (LMCA) in a series of patients with an intermediate pre-test likelihood of CAD, based on an 'intention-to-diagnose' analysis.

Methods

Patient selection

We prospectively enrolled 30 consecutive patients referred to our cath labs between March and August 2007 to undergo elective invasive coronary angiography for suspected CAD. Patients were considered eligible for inclusion if they had an intermediate pre-test likelihood of CAD as defined by: 1) ischemic-type chest pain or other symptoms suggestive of myocardial ischemia in the absence of a positive stress test or with an equivocal stress test for myocardial ischemia or 2) asymptomatic patient with a positive stress test. We excluded patients with a history of CAD as defined by significant coronary stenosis shown in prior coronary angiogram, prior myocardial infarction, prior percutaneous coronary intervention, or prior coronary artery bypass surgery. We also excluded patients with atrial fibrillation and those at risk for iodinated contrast agents (dye allergy or elevated serum creatinine > 1.8 mg/dL). Before inclusion, an informed written consent was obtained from each patient after full explanation of the study protocol, and the study protocol was reviewed and approved by our local institutional human research committee as it conforms to the ethical guidelines of the 1975 Declaration of Helsinki, as revised in 2002.

Definition of risk factors

The presence of hypertension was defined as a systolic blood pressure ≥ 140 mm Hg and/or a diastolic blood pressure ≥ 90 mm Hg, previously recorded by repeated non-invasive office measurements, which lead to life-style modification or antihypertensive drug therapy. The presence of diabetes mellitus was defined as a fasting plasma glucose ≥ 126 mg/dL, and/or a two-hour postload glucose ≥ 200 mg/dL, or specific anti-diabetic drug therapy. Dyslipidemia was defined as an LDL cholesterol > 100 mg/dL, and/or a serum triglycerides > 150 mg/dL, and/or an HDL cholesterol < 40 mg/dL in men and < 50 mg/dL in women.

MSCT, image acquisition

MSCT examinations were performed with a 64--slice scanner (Aquilion 64, Toshiba Medical Systems, Otawara, Japan). First, a non-contrast-enhanced scan was performed prior to MSCT coronary angiography to assess the total coronary calcium burden. For this initial scan, collimation was 4 × 3.0 mm and gantry rotation time 500 ms. Tube voltage and tube current were 120 kV and 200 mA, respectively.

The scan parameters for the standard examination were: collimation 64 × 0.6 mm and rotation time 370 ms. Tube current and tube voltage were 680 mA and 120 kV respectively, with a 0.24 pitch. The total amount of contrast (Iopromide, Ultravist® 300, 300 mg I/mL, Bayer HealthCare Pharmaceuticals Inc., Wayne, Germany) was 80–120 mL injected into an antecubital vein, followed by a 50-mL saline chaser, both injected at a rate of 5 mL/s. Automated detection of peak enhancement in the aortic root was used to time the scan. In all patients, imaging was performed with breath held in inspiration and under retrospective electrocardiographic gating. In patients with a heart rate > 65 beats/minute, beta-blocking agents were administered prior to MSCT imaging if no contraindications for beta--blockade were present. To assess the presence of coronary artery plaques, reconstructions were generated in diastole (typically 75% of the cardiac cycle). Slice thickness was 0.5 mm with an increment of 0.3 mm. In case of motion artifacts, additional reconstructions were explored at different time points of the R-R interval. Thereafter, the axial data sets were transferred to a remote workstation (Wizard, Siemens Medical Solutions, Forchheim, Germany) for post-processing and subsequent interpretation.

MSCT, image interpretation

All data was evaluated on the remote workstation using dedicated software. Two experienced independent investigators, blinded to clinical data, evaluated the contrast-enhanced computed tomo-

graphy scans by assessment of axial slices, as well as post-processing images, including: multiplanar reformations, maximum intensity projections, and volume rendering technique. Orientated along the heart axis, the thin-slab (5 mm thickness, 1 mm increment) maximum intensity projections were reconstructed perpendicular to each other, resulting in the traditional cardiac short- and long-axis views, as well as the 'four-chamber' view. A semi-automatic analysis tool was used for the assessment of severity of LMCA stenosis on curved multiplanar reformations and cross-sections orthogonal to the vessel. Significant stenosis of the LMCA was defined by at least 50% luminal diameter obstruction. According to an 'intention-to-diagnose'-based analysis, arteries with inconclusive segments were considered as significantly diseased.

Invasive coronary angiography

All patients underwent selective left and right coronary arteriography using the standard technique within one week of MSCT examinations. Angiographic data was retrospectively analyzed by a single expert independent interventionalist, blinded to both the clinical data and the results of MSCT coronary angiography. No intracoronary pharmacologic agents were given. Significant stenosis of the LMCA was defined as at least 50% luminal diameter obstruction seen in two different projections. In lesions with borderline significance, an automated edge detection system (Integris 3000, Philips Medical Systems, the Netherlands) was applied to determine lesion severity.

Statistical analysis and study endpoint

The analysis of data was performed on an 'intention-to-diagnose' basis, including all enrolled patients. In this regard, stenotic segments determined as inconclusive by MSCT angiography because of extensive coronary calcification or severe motion artifacts were considered as significantly diseased by MSCT.

The primary endpoint of the study was the accuracy of MSCT angiography to detect significant stenosis of the LMCA, with reference to invasive angiography. Patients were classified as having significant stenosis of the LMCA if they had at least 50% luminal obstruction by invasive angiography, which was regarded as the standard of reference.

All continuous variables were presented as mean ± standard deviation, if they were normally distributed. Data was tested for normal distribution using the Kolmogorov-Smirnov test. Categorical variables were described with absolute and relative (percentage) frequencies. The sensitivity, specificity, positive and negative predictive values and diagnostic accuracy were calculated according to the standard definitions. Analyses were performed with SPSS version 12.0 statistical package (SPSS Inc., Chicago, Illinois, USA).

Table 1. Baseline characteristics of the study series (total cohort: n = 30).

Age (years)	52.6 ± 6.3
Males	24 (80%)
Diabetes	15 (50%)
Hypertension	26 (86.7%)
Smoking	19 (63.3%)
Dyslipidemia	15 (50%)

Continuous variables are presented as mean ± standard deviation, while categorical variables are presented as numbers (percentage).

Results

Baseline clinical characteristics

A total of 30 consecutive patients were prospectively enrolled in the current study. Table 1 shows the baseline clinical characteristics of the whole series. The mean age was 52.7 ± 6.3 years, 24 (80%) being males. Among the series patients, 19 (63.3%) were smokers, 26 (86.7%) were hypertensive, 15 (50%) were diabetic, and 15 (50%) had dyslipidemia. The mean Agatston calcium score was 227 ± 688.

Angiographic data

Based on the aforementioned definition, three (10%) patients had significant stenosis of the LMCA by invasive coronary angiography. Moreover, 18 (60%) patients had significant stenosis of the left anterior descending artery, 11 (36.7%) patients had significant stenosis of the right coronary artery, and three (10%) patients had significant stenosis of the circumflex artery.

On the other hand, four (13.3%) patients were categorized as having significant stenosis of the LMCA by MSCT coronary angiography. MSCT coronary angiography was able to detect significant LMCA stenosis with a sensitivity of 100%, specificity of 96.3%, positive and negative predictive values of 75% and 100% respectively, and a diagnostic accuracy of 96.7%.

Moreover, no patient reported any clinical events during the period from MSCT examinations to invasive coronary angiography.

Discussion

The current study has demonstrated that MSCT angiography was able to identify significant stenosis of the LMCA with a high diagnostic accuracy in patients with an intermediate pre-test likelihood of CAD, based on an 'intention-to-diagnose' analysis. The negative predictive value of 100% reliably ruled out patients with significant LMCA disease in this patient category.

Invasive coronary angiography still remains the 'gold standard' for diagnosis of CAD. In this context, significant CAD is still being excluded by this invasive technique in a large proportion of patients with an intermediate pre-test probability of CAD. To avoid 'unnecessary' invasive testing in this 'not-a-high-risk' patient category, an accurate reproducible, yet safe, non-invasive diagnostic modality is highly desirable. Several prior studies demonstrated the high diagnostic accuracy of MSCT angiography to detect significant (50%) coronary stenosis [9–15]. However, a major limitation of these studies was the enrollment of patients with a wide spectrum of pre-test probabilities of having CAD. Furthermore, patients with already-known CAD, including those with prior percutaneous coronary intervention and those who underwent coronary bypass surgery, were also enrolled [9–15]. On the contrary, the current study has focused on patients an intermediate pre-test likelihood of having CAD, a category in which the diagnostic value of a non-invasive technique would be greatest, and hence, the implementation of this novel technology would be most rewarding.

Stress imaging studies, such as stress myocardial perfusion imaging with radioisotope scintigraphy or dobutamine stress echocardiography, are widely used as non-invasive diagnostic tools for diagnosis/ruling out of significant CAD in patients with low or intermediate pre-test likelihood of coronary disease [16, 17]. Nevertheless, many patients risk developing myocardial infarction, even sudden cardiac death, when exposed to the fairly arduous stress inherent to exercise [18]. Therefore, employing a non-invasive technique for appropriately triaging patients with angina, to further invasive diagnostic work-up mandates an adequately high safety profile of the technique adopted. In this sense, MSCT angiography, being devoid of stress, would offer an excellent non-invasive diagnostic tool for stratifying patients on the basis of their need for invasive coronary angiography. Furthermore, visualization of atheromatous plaques in the LMCA beforehand would add to the safety of the ensuing invasive angiography procedure. Deep catheter insertion in the LMCA during invasive coronary angiography might inadvertently disrupt an ostial or very proximal atheroma, especially if the catheter tip was not coaxial with the LMCA trunk, ending in a catastrophic dissection of the LMCA [19, 20]. The excellent negative predictive value of MSCT to rule out a LMCA atheroma (100%) provides an efficient 'safety net' for reassuring the operator during invasive angiography about the absence of such an 'obstacle to pass'. This valuable piece of information is obviously not offered by the various stress imaging studies. Additionally, characteristics inherent to stress imaging studies limit definite exclusion of coronary atherosclerosis, since non-obstructive atheromatous plaques cannot be excluded. There is a poor association between the amount of atherosclerotic burden and the occurrence of clinical events [21]. Therefore, these non-obstructive plaques (not detected by stress imaging studies) might be the 'seat' of plaque ulceration and thrombosis with the ensuing occurrence of acute coronary syndrome.

The 'intention-to-diagnose'-based analysis adopted in the current study, entailing the assignment of 'inconclusive segments' as significantly diseased ones might have reduced the specificity and the positive predictive value of MSCT to diagnose significant LMCA stenosis (96.3% and 75% respectively). Extensive coronary calcification was previously identified as a substantial problem for the interpretation of MSCT coronary angiograms and the detection of coronary stenoses, essentially due to the blooming effect and beam hardening [10].

Clinical implications

The extremely high sensitivity and negative predictive value of MSCT coronary angiography to detect significant LMCA stenosis in patients with an intermediate pre-test likelihood of CAD, as demonstrated in the current study, would provide an attractive means of ruling out this high-risk condition in this patient category. A normal LMCA by MSCT coronary angiography virtually excludes LMCA stenosis by invasive coronary angiography. Even when MSCT coronary angiography demonstrates significant disease of other coronary arteries/segments, exclusion of LMCA disease would provide reassurance to the operator during invasive coronary angiography that no 'obstacles' remain in his way to inserting the catheter into the LMCA. On the other hand, visualization of an atheromatous plaque in the LMCA would set a 'red-light flash' that maximum care during cannulation of the LMCA should be taken.

Limitations of the study

Our findings are based on a single center study with a relatively small sample size of the cohort, a fact that makes it difficult to generalize our results to all patients with an intermediate pre-test likelihood of CAD. Multi-center studies employing the same protocol and examining a larger number of patients are needed. Moreover, it is uncertain that the results of the current study can be safely extrapolated to patients with high or low pre-test likelihood of CAD. In addition, imaging of adequate quality requires patients with stable and preferably lower heart rates, resulting in a frequent need for the administration of beta blocking agents prior to MSCT angiography. Limitations inherent to the technique include the administration of a potentially nephrotoxic contrast medium and the associated radiation exposure. Despite the application of radiation dose-saving algorithms, the radiation dose estimates are almost doubled with 64-slice MSCT angiography as compared to the old 16-slice systems. This increase in dose, however, resulted in a significant reduction in the number of inconclusive segments, with a subsequent improvement of the test specificity to detect significant coronary stenosis.

Conclusions

In patients with an intermediate pre-test likelihood of CAD, MSCT coronary angiography provides an accurate diagnostic modality for detection of significant LMCA stenosis, with reference to invasive coronary angiography. Its extremely high negative predictive value in this regard provides an attractive means of ruling out this high-risk condition in such an intermediate-risk patient category.

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