Multi-detector Coronary CT Angiography in Comparison with Invasive Coronary Angiography in the evaluation of Significant Coronary Artery Stenosis

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الخلاصة

خلفية الموضوع: ان المفراس الحلزوني المتعدد يسمح بتحديد الكالسيوم المتعلق في الشرايين التاجية , وبعد إضافة الصبغة عن طريق الوريد يمكن رؤية تجويف الشرايين التاجية. هناك فكرة شائعة انه عدم وجود الكالسيوم في الشرايين التاجية يجعل احتمالية وجود تضيقات مهمة قليل جدا لذالك فان مفراس الشرايين التاجية يعتبر من الطرق الواعدة في تشخيص تصلبات الشرايين التاجية لكن على أية حال فان حركة القلب والتكلسات تعيق وضوح رؤية الشرايين في المفراس.

الأهداف: لمقارنة قابلية المفراس الحلزوني في تحديد تضيقات الشرايين التاجية مع قسطرة الشرايين التاجية.

المرضى والطرق: دراسة مقطعية في المستشفى شملت 65 مريض من الذين قاموا بمراجعة المركز العراقي لامراض القلب (بغداد) ومركز شهيد المحراب لامراض القلب(بابل) للفترة من حزيران 2012 الى اذار 2015 الذين يعانون من الم الصدر وتنطبق عليهم صفات استعمال المفراس . المرضى الذين لديهم تضيقات 50 % واكثر بواسطة المفراس تم اجراء قسطرة الشرايين التاجية لهم. مجموع 450 شريان رئيسي وفرعي تم تحليلها .

النتائج: المفراس اثبت نتائج الحساسية ,التحديد , القيمة التنبؤية الموجبة والقيمة التنبؤية السالبة عندما قورنت مع نتائج القسطرة 71%, 69,5%, 82% و 67% على التوالي للشرايين التاجية الاولية. و 56%, 97%, 62%و 95% على التوالي للشرايين التاجية الثانوية. النسبة العامة لحساسية المفراس ونسبة التحديد لكل الشرايين التاجية وتفرعاتها هي 64% و83 % على التوالي وقيمة تنبؤية موجبة 72,5%و قيمة تنبؤية سالبة 81%.

الاستنتاجات: ان نسبة حساسية المفراس الحلزوني المتعدد ونسبة التحديد والقيمة التنبؤية الموجبة والسالبة لتضيقات الشرايين التاجية هي قليلة مقارنة مع نتائج قسطرة الشرايين التاجية.

Abstract

Background: Multi-detector CT angiography (MDCTA) allows detection of coronary artery calcium (CAC) and after contrast injection, visualization of the coronary artery lumen. It is commonly assumed that the absence of coronary calcification makes the presence of obstructive coronary lesions highly unlikely. Coronary computed tomographic angiography (CCTA) is a promising way for diagnosis of coronary artery lesion; however, image quality is still impaired by motion artifacts and calcifications.

Objectives: To compare the ability of multi-slice coronary CT angiography (MSCCTA) with invasive coronary angiography (ICA) for detection of significant coronary artery stenosis.

Patients and methods: It is hospital-based cross sectional study, enrolled 65 patients who attended to Iraqi Center for Heart Disease (Baghdad) and Shaheed Al-Mehrab Cardiac Center (Babylon) from June-2012 to March-2015 complaining from chest pain and fulfill the appropriate use criteria (AUC) for CCTA. Patients who underwent MSCCTA, with lesions causing ≥ 50% stenosis were subsequently studied by ICA. A total of 450 native main vessels and secondary branches were analyzed by single blind observer.

Results: CCTA demonstrated a sensitivity, specificity, positive predictive value (PPV) and a negative predictive value (NPV), when compare with ICA, of 71.5%, 69.5%, 82.4%,67.12%; respectively for primary coronary arteries; and 56.25%, 97%, 62.5%, 95.25%, respectively for secondary coronary arteries. Overall sensitivity and specificity for all coronary arteries and their branches were 64% and 83.3% respectively; with a positive predictive value of 72.5%, and a negative predictive value of 81.1%.

Conclusions: The sensitivity, specificity, PPV and NPV of MSCCTA in the evaluation of significant coronary artery disease (CAD) were low compared with ICA.

Introduction

Coronary angiography has advanced to become a fast and safe investigation for diagnosis of CAD. In some patients are well aware of the minimal risk and the discomfort of the procedure. Therefore there is need for a noninvasive method to demonstrate the coronary arteries in a way that would allow the triage of patients referred to cardiac catheter.[1]

Conventional coronary angiography (CCA) reveals the severity, location and extent of coronary artery stenosis, which are potent predictors and identifies patients with high risk who may get usefulness from revascularization. Thus, ICA, despite the complications, remains the standard method for the diagnosis of the CAD.[2]

The association between vascular disease and vascular calcification has been well known for several years.[3] In both men and women, CAC detected by CT is highly sensitive for the presence of ≥50 percent angiographic stenosis.[4] Many years ago, electron-beam CT was introduced, and its major clinical use has been to quantify coronary calcium as a surrogate marker for the presence of coronary atherosclerosis. Extensive CAC may be present before the plaque burden begins to encroach upon the vessel lumen, and leads to overt coronary stenosis.[5]

The most widely used and best-established measure of CAC for assessment of the diagnostic and prognostic value of electron beam computed tomography (EBCT) scanning is the Agatston score. The amount of calcium present in the coronary arteries is scored according to the Agatstone scale,[6] as follows:

- 0-no identifiable disease.
- 1 to 99-mild disease
- 100 to 399-moderate disease
- 400 and higher-sever disease

Volume score and calcium mass, are often reported and may prove superior to the Agatston score, but have been less well studied.[6] In contrast to the luminographic approach of CCA, CT angiography is a non-invasive cross-sectional or tomographic imaging technique. CTA allows direct visualization of the coronary artery wall and burden of atherosclerosis.[7]

The spatial resolution of CT is continuously improving, resulting in a current 64-slice multi-detector CT. Recently, the dual-source multi-detector CT (DSCT) was released, further improving the temporal resolution.[8] Beginning with the introduction of 4-slice spiral CT systems in 2000, rapid and revolutionary technological advances in the spatial and temporal resolution of multi-slice CT have facilitated practical CCTA.(9) AUC for cardiac computed tomography were first published in 2006 from 8 specialty societies, including the American College of Cardiology and American College of Radiology, with specific indications.(10)

Aims of the study

To compare the sensitivity, specificity, PPV, and NPP of CCTA using 64-MSCCTA with ICA in the evaluation of significant CAD.

Patients and methods

This hospital based cross sectional study enrolled 65 patients who attended to Iraqi Center for Heart Disease (Baghdad) and Shaheed Al-Mehrab Cardiac Center (Babylon) from June-2012 to March complaining from chest pain and/or fulfill the AUC for CCTA. Electrocardiography (ECG), treadmill exercise test (TMT) and echocardiography are obtained during the preliminary steps for risk stratification of the patients. Body mass index (BMI) was calculated .

Patients who had abnormal MSCTA findings (only those with calcium score ≤ 400 Agatstone underwent MSCCTA), with at least one stenosis of minimally 50% diameter; were subsequently underwent conventional evaluation by ICA, for further verification. The main indications for CCTA in this study were as follow, inclusive criteria:

1. Patients with chronic stable angina and have either:
   A. Un-interpretable ECGs (intermediate pretest probability), or
   B. Unable to exercise (intermediate pretest probability).
2. TMT results:
   A. Intermediate risk.
   B. Normal or inconclusive TMT with continued symptoms.
3. Pre-operative assessment for non-cardiac surgery.

Exclusion criteria:

1. Patients who had history of allergy to iodinated contrast.
2. Baseline renal insufficiency (serum creatinine ≥1.7 mg/dl).
3. Irregular cardiac rhythm (atrial fibrillation and frequent ventricular ectopics).
4. Resting heart rate> 65 beats/min (despite beta-blockers).
5. Resting systolic blood pressure < 100 mm Hg.
6. Contraindication to beta-blocker, calcium-channel blocker, or nitroglycerin.

CCTA image acquisition and interpretation

The patients underwent CCTA before conventional ICA. All CCTA scans were performed with a Brilliance CT 64-multidetector scanner BRS 4 system (Philips Healthcare 2010). All patients were in normal sinus rhythm at the time of the CCTA scan. Individuals presenting with baseline heart rates >65 beats/min were administered oral beta-blocker therapy. Intravenous administration of metoprolol at 5 mg increments to a total possible dose of 15 mg to achieve a resting heart rate ≤ 65 beats/min. Patients with calcium score ≤ 400 Agatstone underwent angiography by MSCCTA.

A timing bolus (using 10 to 20 ml contrast) was performed to detect time to optimal contrast opacification at a level immediately superior to the ostium of the left main artery. Nitroglycerine 0.4 mg sublingually was administered immediately before contrast injection. Data sets acquisition starts while the patients hold their breath for 20-30 seconds: a single breath hold. During acquisition, non- iodinated contrast was injected using a dual-phase contrast protocol:80-100 ml iohexol, followed by a 50-ml saline flush (flow rate 5 ml/sec).

All the vessels, regardless of size, including the main coronary arteries, their secondary branches were evaluated for degree of stenosis. Lesions causing ≥ 50% occlusion by quantitative measurements were considered significant; patients having such lesions were referred for conventional ICA.

ICA image acquisition and interpretation

Selective ICA was performed by standard transfemoral arterial catheterization (Seldinger´s technique). A minimum of 8 projections were obtained (minimum of 5 views for the left coronary artery system and minimum of 3 views for the right coronary artery system). All ICA images were interpreted by an interventional cardiologists blinded to all patient characteristics and CCTA results. All angiograms were evaluated by quantitative coronary analysis with automated vessel contour detection and manual correction. The catheter was used for calibration (Quantitative Coronary Analysis, Philips Medical Systems). Lesions with a diameter stenosis ≥ 50% were considered to be significant lesions. If a coronary vessel segment contained more than one lesion, the most severe lesion within the segment determined the diagnostic accuracy of the assessment.

Data Analysis

For the vessel-based analysis, a true-positive was defined as the presence of ≥1 coronary artery segment considered to have an obstructive lesion by both CCTA and ICA in a single arterial system. Four arterial systems were predefined and consisted of the: 1) left main artery (LMT) 2) left anterior descending artery (LAD) inclusive of diagonal branches 3) left circumflex artery (LCX) inclusive of obtuse marginal (OM); and 4) right coronary artery (RCA) inclusive of posterior descending artery (PDA) and right-sided postero-lateral ventricular (PLV) branches. Ramus intermediate arteries were considered to be the first OM branch.

Statistical analysis

Statistical analysis was carried out using an SPSS version 18. Categorical variables were presented as frequencies and percentages. Sensitivity defined as the probability that an individual with the disease will test positive. Specificity defined as the probability that an individuals without the disease will test negative. PPV is the probability that a positive test correctly identifies an individuals who actually have the disease. NPV is the probability that a negative test correctly identifies an individuals who does not have the disease.

Results

There were a 65 patients who enrolled in this study. Male represent (57%) while female represent (43%) of study population. The overall mean age of the patients was 58.2 ± 10.57 years.The overall mean calcium score was 247 ± 108.18. (table 1 and 2).

Table 1 : Distribution of study population by sex

Sex	Number	%
Male	39	57
Female	26	43
Total	65	100

Table 2: The overall mean ± standard deviation (SD) for selected variables

Variable	Mean ± SD
Age (y)	58.2 ± 10.57
Serum creatinine (mg/dl)	0.8 ± 0.14
Agatston coronary artery calcium score	247.7 ± 108.18
Heart rate at time of acquisition (bpm)	58 ± 4.8
BMI (kg/m^2)	28.1 ± 2.85

Figure 1 shows the distribution of patients by indication of MSCT coronary angiography.

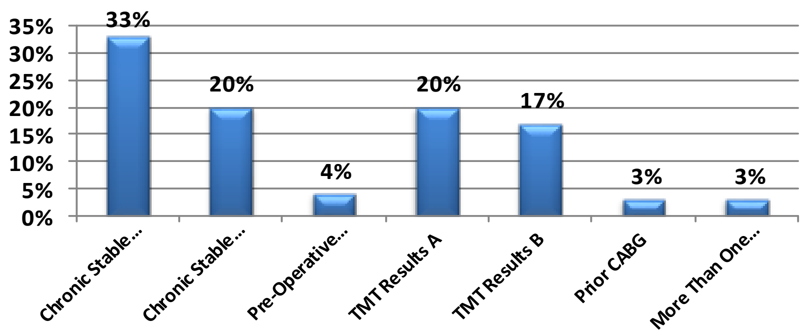

Figure 1: Distribution of patients by indication of MSCT coronary angiography.

Chronic stable angina: A (Un-interpretable ECG). Chronic stable angina: B (unable to exercise). TMT results: A (intermediate risk). TMT results B (normal or inconclusive TMT with continued symptoms).

A total (450) native primary and secondary vessels and were analysed by using non invasive coronary angiography using MSCCTA and invasive coronary angiography. In Comparison to invasive coronary angiography, the sensitivity, specificity, PPV and NPV for MSCCTA for native primary, secondary coronary arteries are describe in tables below.

Table 3 shows the sensitivity, specificity, positive and negative predictive value for each native primary vessel.

For the LMT the sensitivity of MSCCTA to detect coronary obstructive disease was (75%) that mean the MSCCTA was able to detect 75% of patients with coronary obstructive disease correctly, while its specificity was (100%) that mean the MSCCTA was able to detect all healthy persons correctly. The PPV was (100%) that means all patients with positive MSCCTA are more likely to have coronary obstructive disease, while NPV was (96%), which means that 96%

of those with negative results are more likely to be healthy.

For LAD, the sensitivity of MSCCTA to detect coronary obstructive disease was (86%) that mean the MSCCTA was able to detect 86% of patients with coronary obstructive disease correctly, while its specificity was (28%) that mean the MSCCTA can detect only 28% of healthy persons correctly. The PPV was (80%) that means 80% of patient with positive MSCCTA are more likely to have coronary obstructive disease, while the NPV was (40%), which means that 40% of those with negative results are more likely to be healthy.

For LCX, the sensitivity of MSCCTA to detect coronary obstructive disease was (50%) that mean the MSCTA was able to detect half of patients with coronary obstructive disease correctly, while its specificity was (90%) that mean the MSCCTA was able to detect the majority of healthy persons correctly. The PPV was (71%) that means (71%) of patients with positive MSCCTA are more likely to have coronary obstructive disease, while the NPV was (78%), which means that 78% of those with negative results are more likely to be healthy.

For RCA, the sensitivity of MSCCTA to detect coronary obstructive disease was (75%) that mean the MSCCTA was able to detect three quarters of patients with coronary obstructive disease correctly, while its specificity was (60%) that mean the MSCCTA was able to detect only 60% of healthy persons correctly. The PPV was (78.9%) that means nearly three quarters of patients with positive MSCCTA are more likely to have coronary obstructive disease, while NPV was (54.5%), which means that nearly half of those with negative results are more likely to be healthy.

Table 3: Comparison of MSCCTA finding versus the ICA finding for primary vessels.

Parameters	LMT (%)	LAD (%)	LCX (%)	RCA (%)
Sensitivity	75	86	50	75
Specificity	100	28	90	60
PPV	100	80	71	78.9
NPV	96	40	78	54.5

Table 4 shows the sensitivity, specificity, PPV and NPV for each native secondary vessel including the diagonal branches of LAD, obtuse marginals of the LCX and PDA and PLV branches of RCA. For the diagonal artery, the sensitivity of MSCCTA to detect coronary obstructive disease was (50%) that mean the MSCCTA was able to detect half of patients with coronary obstructive disease correctly while the specificity of MSCCTA was (100%) that mean the MSCCTA was able to detect all healthy persons correctly.

The PPV was (100%) that means all patients with positive MSCCTA are more likely to have coronary obstructive disease and the NPV was (96%), which means that the majority of those with negative results are more likely to be healthy.

For OM artery the sensitivity of MSCCTA to detect coronary obstructive disease was (25%) that mean the MSCCTA was able to detect quarter of patients with coronary obstructive disease correctly meanwhile, its specificity was (96%) that mean the MSCCTA was able to detect the majority of healthy persons correctly. The PPV value was (50%) that means half of patients with positive MSCCTA are more likely to have coronary obstructive disease, while the NPV was (89%), which means that 89% of those with negative results are more likely to be healthy.

For PDA branch the sensitivity of MSCCTA to detect coronary obstructive disease was (50%) that mean the MSCCTA was able to detect half of patients with coronary obstructive disease correctly, while the specificity of MSCCTA was (96%) that mean the MSCCTA was able to detect the majority of healthy persons correctly. The PPV was (50%) that means half of patients with positive MSCCTA are more likely to have coronary obstructive disease, while the NPV value was (96%) which means that the majority of those with negative results are more likely to be healthy .

For PLV branch the sensitivity of MSCCTA to detect coronary obstructive disease was (100%) that mean the MSCCTA was able to detect all patients with coronary obstructive disease correctly, while the specificity of MSCTA was (96.5%) that mean the MSCTA was able to detect the majority of healthy persons correctly. The PPV was (50%) that means half of patients with positive MSCCTA are more likely to have coronary obstructive disease, while the NPV was (100%) which means that all those with negative results are more likely to be healthy.

Table 4: Comparison of MSCCTA finding versus the ICA finding for secondary vessels.

Parameters	Diagonal (%)	OM (%)	PDA (%)	PLV (%)
Sensitivity	50	25	50	100
Specificity	100	96	96	96.5
PPV	100	50	50	50
NPV	96	89	96	100

Table 5 shows that, the sensitivity, specificity, PPV and NPV for total primary and total secondary vessels. For primary vessels , the sensitivity of MSCTA to detect coronary obstructive disease was (71.5%) that mean the MSCTA was able to detect approximately 72 % of patients with coronary obstructive disease correctly , meanwhile the specificity of MSCTA was (69.5%) that mean the MSCTA was able to detect approximately 70% of healthy persons correctly . The PPV was (82.4%) that means nearly 82% of patients with positive MSCTA are more likely to have coronary obstructive

disease while the NPV was (67.12%), which means that 67% of those with negative results are more likely to be healthy.
For secondary vessels , the sensitivity of MSCTA to detect coronary obstructive disease was (56.25%) that mean the MSCTA was able to detect approximately half of patients with coronary obstructive disease of secondary vessels correctly , meanwhile the specificity of MSCTA was (97%) that mean the MSCTA was able to detect the majority of healthy persons correctly . The PPV was (62.5%) that means approximately (63%) of patients with positive MSCTA are more likely to have coronary obstructive disease while the NPV was (95.25%) which means that the majority of those with negative results are more likely to be healthy.

Table 5: Comparison of MSCTA finding versus the ICA finding for total primary and secondary vessels.

Parameters	Primary (%)	Secondary (%)	All vessels (%)
Sensitivity	71.5	56.25	63.87
Specificity	69.5	97	83.25
PPV	82.4	62.5	72.45
NPV	67.12	95.25	81.1

Discussion

An earlier meta-analysis of individual 64-MDCT studies demonstrated a sensitivity of 96% and specificity of 73%.[11] Although the number of coronary artery segments considered non-evaluable has decreased with use of 64-multi-detector row CCTA compared with older-generation MDCT scanners.[12] In our study, CCTA diagnostic performance was based upon the totality of all coronary artery segments.
Our study yields a sensitivity of 71.5%, a specificity of 69.5%, a positive predictive value of 82.4%, and a negative predictive value of 67.12% for primary vessels and a sensitivity of 56.25%, a specificity of 97%, a PPV of 62.5% and a NPV of 95.25% for secondary branches.
In a 2008 meta-analysis, 64-slice CCTA had a sensitivity of 99% and NPV of 100% for patient –based detection of significant CAD. However the specificity has been lower than the sensitivity in most studies, and false positive results are possible, particularly in patients with high calcium score.[13]
In the ACCURACY prospective multicenter trial of patient with chest pain without known CAD and intermediate disease prevalence, 64-slice CCTA had a patient-based sensitivity of 94% and a specificity of 83% in detecting stenosis of 70% or greater (comparable values were seen at a 50% stenosis level). Patients with high calcium score were not excluded from the study. Calcium score greater than 400 reduced specificity significantly. The NPV of CCTA was 99%.[14]
In the CORE 64 prospective multicenter trial of patients with symptomatic CAD referred for conventional coronary angiography, 64-slice CCTA had a patient-based sensitivity of 85% and specificity of 90% (excluding patients with calcium score greater than 600) for detecting stenosis 50% or greater. However, the NPV of 83% in this study was lower than in other studies.[15]
Another analysis for 64-slice scanners (7 studies in 444 patients) confirms greater accuracy, with reported sensitivity and

specificity of 98% and 93%, respectively.[16]

In our study, heart rate seems to be of little effect on diagnostic performance of CCTA for detection of ≥50% coronary artery stenosis because the cutoff point for heart rate in our study is ≤ 65 beat/min.

Giesler and Becker demonstrate that heart rate has a major impact on image quality [17] and come to the conclusion that vessel visibility is best for heart rates ≤65 beats/min. The cause for limitation of heart rate can be explained by the temporal resolution of the CT image acquisition and reconstruction system. To avoid this limitation, two basic strategies are possible. Either the gantry rotation speed is increased mechanically to improve the system's temporal resolution of the CT-scanner or negative chronotropic substances such as beta-blockers are to be used to decrease the heart rate to the desired level.

The average BMI of our study patients was 28.1±2.85 kg/m^2, indicating a generally overweight population and obesity is not a major impact on image quality. However, ACCURACY trial results indicate that proper use of current generation 64-multidetector row scanners in obese subjectscan still yield highly accurate results. [18]

Extensive coronary calcium obscures the lumen and may substantially limit analysis of segments or even entire arteries by CCTA. Thus, this technique may be of limited application in patients with a high likelihood of significant coronary calcification, such as the elderly or in patients with prior calcium scores >1,000 Agatston units.[19]

Many studies evaluating CCTA accuracy have been performed in academic centers with expertise in performance and interpretation of CCTA. Therefore, the results of our study might be due to our initial experience in the evaluation of significant coronary artery disease using multidetector CT angiography. [18] Recently published AUC addressing the clinical use of CCTA have suggested that its greatest potential utility may be for the patients with intermediate-risk.[19]

It should be noted that most of the earlier studies evaluating the diagnostic accuracy of CCTA were performed with patients with a generally high prevalence of obstructive coronary artery stenosis. Because disease prevalence may directly affect the characteristics and performance of a diagnostic test, CCTA requires delicate assessment in patients with intermediate risk as proven by American Heart Association (Class IIa). [20]

Study limitations

1. Our study enrolled small number of patients and this might be the major cause for the marked variation in results compared with other studies.In addition, a limited number of patients were referred for CCA on the basis of CTA findings.

2. Our study is a two center design when compared with large multicenter studies and meta-analyses.

3. The reference standard used in the present study was quantitative coronary angiography rather than semi-quantitative assessment of luminal diameter stenosis by ICA, which is more prone to inter-observer variability.

4. No interpreting format was pre-specified for the CCTA readers, who

used a variety of interpretative 3-dimensional post-processing algorithms, which precludes definitive comparison of one CCTA interpretation technique to another.

Conclusion

In our study, the sensitivity, specificity, PPV and NPV of MSCTA in the evaluation of significant CAD were low compared with invasive coronary angiography.

Recommendations

1. Large multicenter studies with large number of patients to evaluate the accuracy of MSCCTA for detection of significant coronary artery disease are suggested.
2. Because disease prevalence may directly impact the characteristics and performance of a diagnostic test, CCTA requires efficacy assessment in patient populations with intermediate rather than high disease prevalence.

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