SIGNIFICANT CORONARY ARTERY STENOSIS IN PATIENTS WITH LOW CORONARY ARTERY CALCIUM SCORE

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ABSTRACT

Background: Coronary artery disease is a major cause of morbidity and mortality. Non-invasive techniques for diagnosis are becoming increasingly popular and multidetector coronary computed tomography has emerged as a promising modality. Quantifying the amount of coronary artery calcium with unenhanced CT calcium score has been shown to be a reliable noninvasive technique for screening risk of future cardiac events. In previous trials low coronary artery calcium score has been shown to rule out coronary artery disease with high predictive value.

Objective: To evaluate the level of agreement between severity of stenosis on CT angiography and calcium burden as measured by dedicated CT protocols for calcium scoring, comparing their results.

Material and Method: The study was conducted at Radiology Department, Shaukat Khanum Memorial Cancer Hospital and Research Centre and Heart and Body Scan Centre, Lahore. Duration of study was 6 months. The study design was a cross sectional survey.

Results: Mean age of patients was 38.65+5.72. Male to female ratio was 2.5:1 (72 males: 27 females).Agreement of low calcium score and insignificant coronary stenosis was found in 78 patients while 22 showed no agreement. Kappa test was applied, p value was recorded. 0.0005. 50% (11 out of 22) of the patients with calcium score of 0 had significant coronary stenosis.

Conclusion: The results of study reveal that absence of calcium or low calcium does not exclude significant coronary stenosis. Depending on presentation, it is recommended to get calcium score and coronary CT angiography done in the same setting.

INTRODUCTION

Coronary artery disease (CAD) is a major cause of morbidity and mortality all over the world including Pakistan and is usually attributable to atherosclerotic obstruction.[1]

The potential benefit of noninvasive coronary angiography is likely to be greatest for symptomatic patients who are at intermediate risk for coronary artery disease (CAD) after initial risk stratification, including patients with equivocal stress tests. Coronary computed tomography angiography (CCTA) is recommended over coronary magnetic resonance angiography (MRA) because of superior diagnostic accuracy. Neither coronary CTA nor MRA is recommended to screen for CAD in patients who have no signs or symptoms suggestive of CAD.[2]

Quantifying the amount of coronary artery calcium with unenhanced CT calcium score has been shown to be a reliable noninvasive technique for screening risk of future cardiac events[3,4] and can be quantified by using the Agatston score.[5] Coronary artery calcium (CAC) scoring has been advocated as a quick, non-invasive, iodinated contrast-free method to assess for the likelihood of obstructive CAD in symptomatic patients based on studies demonstrating very low rates of obstructive disease in patients with a CAC score of 0.[6]

Coronary artery calcium score (CACS) is usually performed as a screening method with the use of low radiation dose scanning techniques. The purpose of the scan is to detect and calculate the calcium density, volume or mass. The total coronary calcium is used as a way of prognosticating and stratifying the risk of CAD. The rationale behind it is that coronary artery calcification is part of the atherosclerotic degeneration of the arterial vessel wall, and coronary atherosclerosis is the only disease associated with calcium in the coronary arteries.

The calcification of the atherosclerotic lesion begins at the stage of fatty streak formation as early as in the second decade of life.[7]The quantity of coronary artery calcium correlates with the burden of atherosclerosis in different individuals, and to some

extent also with different segments of the coronary artery tree in the same individual.[7]

Multidetectorcoronary computed tomography (MDCCT) has emerged as a promising minimally invasive method for detection and exclusion of obstruction in coronary artery disease. MDCCT both detects CAC and allows direct assessment of stenosis with high degree of accuracy.[8,9] In several trials, absence of coronary artery calcium ruled out the presence of significant CAD with high predictive value.[10] CACS <100 are thought to be associated with no obstruction on cardiac catheterization.[8]Calcium score reproducibility is modest, with interscan variability of 10% to 20%, being more reproducible at low heart rates and for higher calcium scores.[11]

The current study is designed to evaluate the level of agreement between severity of stenosis on CT angiography and calcium burden as measured by dedicated CT protocols for calcium scoring, comparing their results. The relevant prognostic information obtained may be useful in initiating, modulating or intensification of appropriate treatment and diagnostic strategies.

MATERIAL AND METHODS

The study was conducted at Radiology Department, Shaukat Khanum Memorial Cancer Hospital and Research Centre and Heart and Body Scan Centre, Lahore. Duration of study was 6 months. The study design was a cross sectional survey.

Sample size of 100 cases was calculated with 95% confidence level, 10 percent margin of error and taking expected percentage of agreement between calcium score and coronary stenosis on CT angiography as 50% in patients with suspected or known coronary artery disease. Non-probability purposive sampling technique was used.

Patients were selected using the following inclusion criteria; age greater than 25 years of age, both sexes, suspected or known CAD, coronary artery calcium score 100 or less, sinus rhythm. The exclusion criteria was having previously undergone coronary stenting or bypass grafts, renal dysfunction or raised serum creatinine greater than 1.5 mg/dl, allergy to iodine or IV contrast and pregnancy.

Data Collection Procedure

Patients with suspected or known CAD referred by physicians for MDCCT,s fulfilling inclusion/exclusion criteria were scanned after obtaining informed consent and demographic history. CT Scan was performed on 64-slice Aquillion (Toshiba Medical System, Japan). For calcification assessment, un-enhanced ECG gated cardiac CT was done. It was followed by CT angiography using non-ionic intravenous contrast medium (lopromide Ultravist, Schering Germany). Reconstruction and interpretation of scans was done on workstation Vitrea 2 version 3.0.9.1 (vital images, Minnesota, USA). A radiologist assessed each segment on non-enhanced CT for amount of calcium using Agatston score (Table 1) and also assessed each segment on contrast enhanced CT for stenosis. The sum of segmental calcium scores was taken. The most significant stenosis > 50% was noted for each vessel and patients. All this information was recorded in a pre-designed proforma.

Data Analysis Procedure

Collected data was entered and analyzed using the statistical software (SPSS) version 12. Quantitative variable like age was presented in the form of mean + SD. Qualitative variable like gender were in the form of frequency and percentages. Agreement between coronary artery calcium score less than 100 and CT angiography for the diagnosis of the significant stenosis > 50% was calculated as frequency and percentages. Kappa statistics were used to determine the strength of agreement between calcium score less than 100 and CT angiography for the diagnosis of significant stenosis

RESULTS

Demographics

Mean age of patients was 38.65+5.72. Male to female ratio was 2.5:1 (72 males: 27 females).

Frequency of Agreement of Low CACS and Insignificant Coronary Stenosis

Agreement of low CACS and insignificant coronary stenosis was found in 78 patients while 22 showed no agreement. Kappa test was applied, p value was recorded. 0.0005.

Relation between CACS and Significant Stenosis

Table 2 shows relationship between low CACS and significant stenosis.

Table 1: Agatson Calcium Scoring

Calcium Score	**Interpretation**
0 – 1	No identifiable atherosclerotic plaque; very low cardiovascular disease; less than 5% chance of presence of coronary artery disease A negative examination
1 – 10	Minimal plaque burden Significant coronary artery disease very unlikely
11 – 100	Mild plaque burden Likely mild or minimal coronary stenosis
101 – 400	Moderate plaque burden Moderate nonobstructive coronary artery disease highly likely
Over 400	Extensive plaque burden High likelihood of at least one significant coronary stenosis (>50% diameter)

Table 2: Relation between CACS and Significant Stenosis (n = 22)

CACS	**No. of patients**	**%**
0	11	50
1 - 30	6	27.27
31 – 60	3	13.63
61 - 90	1	4.55
91 - 99	1	4.55
Total	**22**	**100**

DISCUSSION

CT angiography and CACS can be used to predict the presence or absence of coronary artery disease. Few studies, however, have addressed the ability of CT angiography and CACS (assessed with multi section CT) to demonstrate lesions in individual coronary arteries and the potential limitations of such evaluation.

Although several trials have shown that absence of coronary artery calcium can rule out presence of significant CAD, this has been challenged in recent studies.[8,10,12,19] In one study several CCTA indices were highly correlated, in particular, the coronary obstruction score, the number of involved segments, the severity of CAD score, and the segment stenosis score (all <0.80). Calcium scoring correlated with the number of involved segments and the number of calcified plaques (both < 0.85). However, the study further showed that CCTA scores, taking into account the degree of stenosis and those assessing the extent of atherosclerosis can predict cardiac events significantly better than calcium scoring and clinical risk scores. [13]

We designed this study to evaluate the level of agreement between severity of stenosis on CT angiography and calcium burden as measured by dedicated CT protocols for calcium scoring, comparing their results.

We looked at MDCCT of 100 symptomatic patients with low calcium scores of which 78 had no significant stenosis. Of the remaining 22 with significant stenosis majority had a very low CACS (11 patients had CACS of 0). This was affirmed by other studies as well e.g. Kelly et al reported a population of 325 patients (high risk for CAD or atypical symptoms or abnormal stress test results) with zero CACS undergoing CCTA and CAG. The authors found 167 patients with non-calcified plaques and 18 (5.5%) patients with obstructive CAD. They concluded that an atherosclerotic burden and obstructive CAD may be present in patients with zero CACS and that imaging the vessel wall directly may be helpful to identify noncalcified plaque and guide therapy[14]. In a study by Morita et al 24 patients with CACS of 0 out of 1019(2.4%) were found with significant stenosis.[15]

Akram et al. explored the impact of symptoms in a population of patients with zero CACS.[15]They used CCTA as the reference standard for CACS in detecting obstructive CAD (CAG was not performed extensively). They found that 8.2% of the symptomatic patients with zero CACS had an obstructive coronary artery stenosis. In the asymptomatic patients with zero CACS, there were no obstructive coronary lesions. They concluded that CCTA is better than CACS in symptomatic patients, and CACS is better than CCTA in asymptomatic patients.[16]

Another study studied a very large (n= 1,000) asymptomatic population with CCTA.[17]The mean CACS was very low (Agatston=18), and the prevalence of obstructive CAD was 7.3%. In the subgroup of patients with zero CACS, 4% (40/825) of the patients had non-calcified plaques, with 1.8% (15/825) having

significant or severe obstructive CAD. They concluded that occult CAD cannot be ruled out in the asymptomatic population. Similarly Cademartiri et al extrapolated that there is some obstructive burden of disease in populations with zero CACS and that this prevalence is very much affected by clinical presentation (symptomatic vs. asymptomatic). They found that the noninvasive assessment of arterial segments at CT angiography is useful and results in few misclassifications, but that CACS is best used to identify patients with disease rather than to exclude disease or to localize stenosis to particular arteries or segments. Therefore, CT angiography is likely to be better suited to the detection of new obstructive coronary lesions than is CACS.[18]

On the other hand a recent study showed patients with increasing degrees of CAC had significantly increased severity of angiographic CAD on CCTA. Out of 2406 patients with CACS of 0 2316 had normal vessels, 78 had one vessel CAD, 11 had two vessel CAD and only one patient had one vessel disease. It showed that higher CAC scores were associated with a greater extent of CAD ($P < .001$)[19]

The results of our study in determination of patients who show agreement between low coronary artery calcium score and coronary CT angiography for the exclusion of significant stenosis by using CT Scan on 64-slice Aquilion (Toshiba Medical System, Japan) shows a significant relation with calcium level <100 for stenosis. However, value of CACS as gatekeeper to conventional coronary angiography has been questioned. A significant strength of our study was its prospective nature and thorough analysis of calcium score and coronary artery stenosis. Our limitations were that we could not evaluate prognostic value of calcium score and stenosis as most patients were referred and lost to follow-up. We could not correlate all our findings with conventional coronary angiography, still regarded as gold standard. The reporting physician was also aware of patients calcium score at the time of assessing stenosis.

CONCLUSION

The results of the study reveal that absence of calcium or low calcium does not exclude significant coronary stenosis. Depending on presentation, it is recommended to get calcium score and coronary CT angiography done in the same setting.

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