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Original Article

The Value of Coronary Computed Tomography Angiography in Patients with a High Calcium Score

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Abstract

Background: *We aimed to assess the agreement between coronary computed tomography angiography (CCTA) and invasive coronary angiography (ICA) to determine whether patients with a high coronary artery calcium score (CS) would benefit from CCTA.*

Methods: *This cross-sectional study was conducted on patients suspected of having coronary artery disease. The patients underwent calcium scoring. The total CS and the number of calcified foci were determined. The calcium score index (CSI) was defined, and coronary arteries were evaluated by CCTA. ICA was performed, and reports of ICA were extracted. All the abovementioned variables were compared. For data analysis, the κ coefficient and the ROC curve were used.*

Results: *The study population consisted of 195 patients: 124 men (63.6%) and 71 women (36.4%). The median (IQR) value of CS was 529 (229-1042), ranging from 17 to 4717. In all 195 patients, the concordance between the final impression of CCTA and ICA was 90.2%, while the number and type of involved territories were similar at 57.9%. The highest agreement was seen in the left main and right coronary arteries, whereas the lowest agreement was detected in the left anterior descending and the left circumflex artery. The patients were categorized into different CS groups, and in those with a high CS (>1000), the agreement between CCTA and ICA concerning final impression and involved territories was similar to the whole group of patients.*

Conclusion: *CCTA in patients with a high CS, even exceeding 1000, remains beneficial as the noninvasive available method.*

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Introduction

Cardiovascular risk can be estimated excellently by measuring the total coronary artery calcium score (CS) using a gated non-contrast study.[1] Calcified spots in the walls of coronary arteries constitute a sign of coronary artery disease (CAD). Initially, a fluoroscopic device was used to examine these plaques; nevertheless, subsequent studies showed that computed tomography (CT) scans were more sensitive than fluoroscopy in detecting intravascular calcification.[2,3] Calcification grading in arteries is done based on several criteria. The density and area of calcified plaques are the most significant factors in CS calculation.[4] Numerous studies have investigated the association between CS and CAD and yielded discrepant results.[5] Recent investigations have focused more on changes in this method and factors such as the volume and extent of calcification.

Coronary computed tomography angiography (CCTA) has been accepted as an alternative to invasive coronary angiography (ICA) since it allows a noninvasive evaluation of CAD.[6-8] CS plays a gatekeeper role in obviating the need for or proceeding to CCTA. The diagnostic performance of CCTA in evaluating CAD may be limited in the presence of calcification owing to blooming artifacts. Nonetheless, reports have been controversial regarding the influence of the different grades of coronary artery calcium scoring (CACS) on CCTA accuracy.[9-17]

Previously, the predominant practice was to stop CCTA in patients with a high CS and instead establish new thresholds for stopping or continuing CCTA. More recently, however, positive experiences have been reported concerning patients with a high CS measured with a new generation of machines. Accordingly, a comparison of accuracy between CCTA and ICA with a focus on a high CS is warranted. In the present study, we sought to determine whether there was an index other than CS that could identify patients who would benefit from CCTA. Our experience indicated that CCTA tended to be more conclusive in patients with a high CS and more distributed calcified foci than in those with the same CS but with fewer calcified foci. In this regard, we aimed to evaluate CCTA results in a high CS group and determine whether the distribution of calcification or the number of calcified spots could predict the agreement between CCTA and ICA.

Methods

This cross-sectional study was conducted from 2018 through 2020 at Chamran Hospital, affiliated with Isfahan University of Medical Sciences, Isfahan, Iran. The study was done on patients suspected of having CAD referred to our center to undergo CACS and CCTA. The study protocol was approved by the Research Committee and confirmed by the Ethics Committee (ethics code: 3981024) of Isfahan University of Medical Sciences.

The inclusion criteria consisted of having CACS and CCTA results and undergoing ICA within a short interval (<3 mon) after CCTA. A history of percutaneous coronary intervention or coronary artery bypass grafting, a CS of 0, refusing consent for study participation, and not having ICA reports comprised the exclusion criteria.

The sample size was estimated based on a sensitivity of 90%, with a confidence level of 95% (α=0.05), a margin of error of 0.08, and a prevalence rate of 30% for a high CS among patients. According to our pilot study considering all these items, the sample size was determined to be 180 patients. The study population was recruited based on the inclusion criteria using the census method. Of 385 patients who underwent ICA based on clinical indications at the cardiologist's discretion, 195 patients had available ICA results and were, thus, considered the final study population.

CACS was performed as non-enhanced gated CT (parameters: 120 kV, 55 Ma, and 2.5 mm slice thickness). All data were evaluated using semiautomated software (Extended Brilliance Workspace; Philips Medical Systems) to identify calcium spots needing manual marking by the radiologist. All spots were automatically calculated to a summed CS. Pixels with a density of at least 130 HU and a minimum area of 1.03 mm^2 were identified as calcium spots.

For each study, CS was calculated using the methods of Agatston et al,[18] and the number of spots or calcified foci (lesions) was determined. The total CS was divided by the number of lesions and was defined as the calcium score index (CSI). The subjects were categorized as Group I (CS=1–100), Group II (CS=101–400), Group III (CS=401–1000), and Group 4 (CS>1000).[19]

CCTA was performed with a 256-slice multidetector CT scan (Brilliance 256, Philips Medical System), and a special workstation was used for reporting. The same device was utilized for all the enrolled cases. The imaging protocol included a collimation of 96 to 128 mm, a detector size of 0.625 mm, a rotation time of 0.27 milliseconds, a voltage of 120 kV, and a radiation quantity of 180 to 200 milliampere seconds. If a patient had a high heart rate (>75 bpm), an oral β-blocker (50–100 mg of metoprolol) was given 1 hour before the examination. Additionally, sublingual nitroglycerin (0.4 mg) was administered 1 minute before acquisition to dilate coronary arteries.

According to the patient's body mass index, 70 to 90 mL of an intravenous contrast medium (Visipaque 320 mg) with a flow rate of 5 to 6 mL/s was injected; then, 40 mL of saline was added with a velocity of 4 mL/s. Ultimately, images were taken in prospective or retrospective conditions (according to the patient's condition). Reconstructions were sent to Philips Workstation to provide CCTA reports. A radiologist expert in cardiac imaging was involved in the evaluation of the CCTA images. All the reconstructed image formats authorized for image analysis contained axial or oblique maximum intensity projections and curved multiplanar reconstructions.

Coronary arteries greater than 1.5 mm in diameter were evaluated based on the coronary artery disease-reporting and data system (CAD-RADS), and the final impression was categorized as CAD-RADS 1 to 5.[20]

Patients with CAD-RADS of 1, 2, or 3 were defined as nonsignificant CAD, whereas those with CAD-RADS of 4 or 5 were categorized as significant CAD.

Three coronary territories were defined as the left anterior descending (LAD) territory (including all parts of LAD and the diagonal arteries), the left circumflex (LCX) territory (including all parts of LCX and the obtuse marginal arteries), and the right coronary artery (RCA) territory (including all parts of RCA, the posterior descending artery, and the posterolateral ventricular artery). The left main coronary artery (LMCA) was interpreted separately.

In addition to the final impression of CCTA as significant or nonsignificant CAD, the number of involved territories was determined and categorized as single-vessel disease, double-vessel disease, and triple-vessel disease, and LMCA was considered involved or noninvolved.

In each territory, the concordance between CCTA and ICA was evaluated, regardless of the final impression.

ICA was performed for each patient according to the standard clinical care and the decision of the cardiologist. Vessel-based standard reports were reviewed by a resident of radiology under the supervision of a cardiologist, blinded to the CCTA reports. The final impressions of ICA (significant vs nonsignificant CAD), the number of involved territories, and LMCA involvement were determined and recorded. Incomplete or nonstandard reports were excluded.

All the above variables were gathered based on the results of both CCTA and ICA. CCTA was defined as diagnostic if an agreement was seen between final CCTA and ICA impressions. CCTA studies were considered adequate if, in addition to the final impression, the involved territories were similar concerning the type and number.

Data analysis was conducted with SPSS, version 16, to evaluate concordance, κ coefficient, sensitivity, and specificity. Continuous data were presented as mean ± standard deviation (SD) or the median (the interquartile range [IQR]) according to the normality distribution of the variable assessed via the Shapiro-Wilk test. The receiver operating characteristic (ROC) curve was used. The significant level was set as 0.05.

Results

The present study analyzed data from 195 cases: 124 men (63.6%) and 71 women (36.4%) with a mean age of 63.68±10.21 years, ranging from 39 to 87.

The median (IQR) value of CS was 529 [229–1042], ranging from 17 to 4717. In all the patients, concordance between CCTA and ICA was 90.2% (κ=0.48) in the final impression and 57.9% (κ=0.40) in the involved territories. Concordance between CCTA and ICA results in terms of the presence or absence of significant stenosis in LMCA, LAD, LCX, and RCA was 95.9% (κ=0.67), 75.9% (κ=0.37), 76.9% (κ=0.52), and 86.7% (κ=0.72), respectively.

Of all 195 patients, 26 had a CS below 100, 53 had a CS between 100 and 400, 65 had a CS between 400 and 1000, and 51 had a CS exceeding 1000.

The mean age in the 4 groups was 57.46, 61.25, 65.31, and 67.00 years, respectively (P<0.001). The diagnostic CCTA and adequate CCTA (according to the definition in the current study) in the different CS groups are shown in Table 1. Concordance in territory involvement (LM, LAD, LCX, and RCA) is presented in Table 2.

CS and CSI were analyzed in relation to diagnostic cases

Table 1. Diagnostic and Adequacy of CCTA Compared With ICA in the Different CS Groups*

CS Group	Diagnostic Cases	Adequate Cases
1-99	25/26 (96) (k=0.866)	17/26 (65) (k=0.444)
100-399	41/53 (77) (k=0.590)	27/53 (51) (k=0.306)
400-1000	63/65 (97) (k=0.734)	41/65 (63) (k=0.429)
>1000	47/53 (89) (k=0.558)	28/51 (46) (k=0.370)

*Data are presented as n (%).

CCTA, Coronary computed tomography angiography; ICA, Invasive coronary angiography; CS, Calcium score; k, Kappa (a statistical measure of inter-rater reliability for categorical variables)

Table 2. Correlation (Agreement) Between CCTA and ICA in Different Territories According to the CS Groups*

CS Group	LM Territory	LAD Territory	LCX Territory	RCA Territory
1-99	26/26 (100) (k=1.0)	17/26 (65) (k=0.282)	22/26 (85) (k=0.662)	26/26 (100) (k=1.0)
100-399	51/53 (96) (k=0.649)	34/53 (64) (k=0.167)	42/53 (79) (k=0.531)	44/53 (83) (k=0.643)
400-1000	64/65 (98) (k=0.792)	56/65 (86) (0.619)	50/65 (77) (k=0.506)	56/65 (86) (k=0.706)
>1000	46/51 (90) (k=0.609)	41/51 (80) (k=0.292)	36/51 (70) (k=0.409)	43/51 (84) (k=0.681)

*Data are presented as n (%).

CCTA, Coronary computed tomography angiography; ICA, Invasive coronary angiography; CS, Calcium score; LM, Left main; LAD, Left anterior descending; LCX, Left circumflex artery; RCA, Right coronary artery; k, Kappa (a statistical measure of inter-rater reliability for categorical variables) considering the final impression, and their ROC curves were drawn (Figure 1). Considering ROC curves, CS was superior to CSI in predicting diagnostic CCTA. A CS of 356 with a sensitivity of 70% and a specificity of 66% and a CSI of 17.5 with a sensitivity of 64% and a specificity of 52% could predict diagnostic tests, or in other words, concordance between the final impression of CCTA and ICA.

Adequate CCTA was 68% in all the patients and 46% in those with a CS above 1000. The accuracy, sensitivity, and specificity of CCTA in patients with a CS exceeding 1000 were 92.16%, 97.7%, and 50%, respectively. Absolute CS or CSI was not significantly predictive of diagnostic or adequate CCTA.

In all the cases, CCTA, in comparison with ICA, had a sensitivity of 92.70%, a specificity of 64.71%, a positive predictive value of 96.49%, a negative predictive value of 45.83%, and an accuracy of 90.26%.

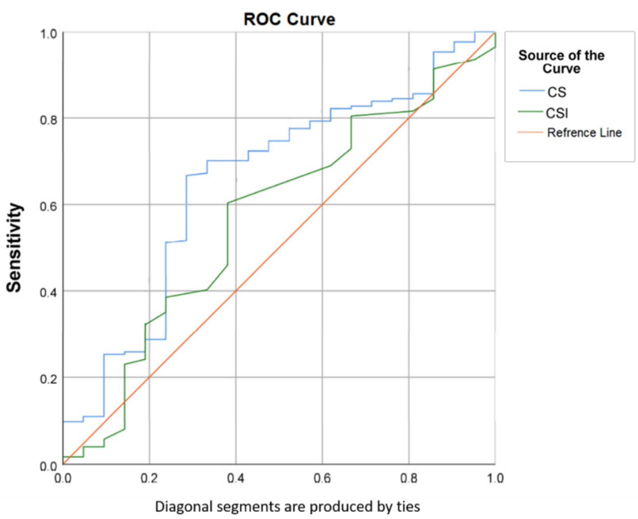

Figure 1. The image presents the receiver operating characteristic (ROC) curve for the diagnostic value of the calcium score (CS) and the calcium score index (CSI).

Discussion

The accuracy of CCTA in our study population, particularly in cases with a high CS, was acceptable. To rephrase, most of our patients had successful or conclusive results. Despite the growing use of CCTA and reported excellent results concerning the high accuracy of CCTA, the negative impact of extensive coronary calcification on the accuracy of the study because of the partial volume and beam-hardening effects is still a concern.[21, 22] While in some cardiac imaging departments, CCTA is canceled in high levels of CS, a large number of such patients undergo this noninvasive examination elsewhere. Indeed, the question remains as to what constitutes the appropriate CS threshold at which to cancel CCTA and replace it with ICA.

We demonstrated an accuracy of 90.26%, a sensitivity of 92.70%, and a specificity of 64.71% for CCTA, compared with ICA, in the study population. The accuracy, sensitivity, and specificity of CCTA in patients with a high CS (>1000) were 92.16%, 97.7%, and 50%, respectively.

The high sensitivity and limited specificity of CCTA have been similarly shown by some previous studies.[23-25] Ahn et al[25] reported that in cases with a CS above 1000, despite a drop in specificity, the accuracy and sensitivity were acceptable. Additionally, they mentioned that even in patients with extensive calcification, unnecessary ICA was avoided. Kwan et al[26] reported a sensitivity of 94% and a specificity of 55%, chiming with our results. The low specificity in our study might be due to selection bias. We did not move most of our patients to ICA after obtaining CCTA results indicating nonsignificant CAD. Further, we were unable to identify a significant number of patients with negative CCTA who had undergone ICA, leading to a decrease in the number of true negative cases in our study group. All ICA examinations were based on the clinical judgment of clinicians, and despite the prospective direction of the investigation, we did not move any patient to ICA merely because of our study.

We defined adequate CCTA to evaluate whether the number of involved territories in CCTA was the same as that in ICA, regardless of the final impression. The rate of adequate CCTA was 57.9%, which means that in almost half of our patients (with an average CS of 780), ICA failed to add more information than CCTA. In the second step, we evaluated agreements in different territories. The highest agreement was for the LMCA (94.8%), with the lowest for LAD and LCX. Kwan et al[26] found the most accurate results for LMCA and the least for LCX, in line with our study. Of 53 patients with a high CS (>1000), the final impression of CCTA was similar to that of ICA in 89%. More noticeably, in 46% of these patients, CCTA was adequate. To restate, almost half the patients with a CS above 1000 had conclusive CCTA (similar to the whole group), and ICA did not change the result.

As mentioned earlier, selection bias was the limitation of our study. Furthermore, because CS is a known risk factor for CAD, it can lead to a higher prevalence of positive CAD, and this case selection could affect the specificity.

Abdulla et al,[27] in a meta-analysis in 2012, suggested that CS thresholds were arbitrary and did not necessarily warrant canceling angiography. Likewise, in a study by Agustin et al,[28] the agreement between CCTA and ICA was not impacted by CACS significantly.

We conducted this study based on the assumption that regardless of the CS value, the number of calcified foci might be significant in predicting CCTA accuracy. In our experience, patients with a very high CS and more distributed calcified spots (resulting in a lower CSI) had more acceptable accuracy in CCTA than those with a higher CS and fewer calcified lesions. This notion seems justified because the more distributed the calcified burden is, the less thickness is considered for each lesion, leading to a diminished beam-hardening effect. We evaluated this hypothesis in the current study. As the ROC curve showed, CSI was not better than CS in predicting the diagnostic rate of CCTA, which may be related to our measuring method.

Since it is justified that the distribution of calcification, as opposed to the absolute value of CS, is beneficial in predicting CCTA results (in terms of being diagnostic), further studies avoiding our limitations are recommended.

Conclusion

The present study showed that CCTA in patients with a high CS, even exceeding 1000, remained beneficial. Considering the invasiveness of conventional coronary angiography, patients should not be deprived of this noninvasive method just because of a high CS.

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