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Prognostic Value of Coronary Artery Calcium Score for Determination of Presence and Severity of Coronary Artery Disease

Authors' Contribution:
A Study Design
B Data Collection
C Statistical Analysis
D Data Interpretation
E Manuscript Preparation
F Literature Search
G Funds Collection

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Summary

Background: There are controversies regarding the usefulness of coronary artery calcium score (CACS) for predicting coronary artery stenosis. The aim of this study was to determine the prognostic value of CACS for determining the presence and severity of coronary artery disease (CAD) in patients with sign and symptoms of the disease.

Material/Methods: In this cross-sectional study, 748 consecutive patients with suspected CAD, referred for coronary computed tomography angiography (CCTA), were enrolled. The mean CACS was compared between patients with different severities of coronary artery stenosis. The association between CACS and different CAD risk factors was determined as well. Different cutoff points of CACS for discriminating between different levels of coronary artery stenosis was determined using receiver operating characteristic (ROC) curves.

Results: The mean CACS was significantly different between different levels of coronary artery stenosis ($P<0.001$) and there was a significant positive association between the severity of CAD and CACS ($P<0.001, r=0.781$). ROC curve analysis indicated that the optimal cutoff point for discriminating between CAD (presence of stenosis) and the non-stenosis condition was 5.35 with 88.6% sensitivity and 86.2% specificity. Area under the curve for different levels of coronary artery stenosis did not have sufficient sensitivity and specificity for discriminating between different levels of CAD severity (<70%).

Conclusions: The study demonstrated that there is a significant association between CACS and the presence as well as the severity of CAD. CACS could have an appropriate prognostic value for the determination of coronary artery stenosis but not for discriminating between different severities of stenoses.

MeSH Keywords: Angiography • Coronary Artery Disease • Multidetector Computed Tomography

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Background

Coronary artery disease (CAD) is one of the most common causes of morbidity and mortality and has a high socio-economic burden. The detection and proper management of CAD in the earlier stages of the disease could reduce the burden of the disease, its related complications, treatment costs as well as improve quality of life of the affected patients [1,2].

Although coronary angiography is considered to be the gold standard method for the evaluation of coronary artery disease and its management, it is invasive. Recently, noninvasive techniques, such as coronary CT angiography (CCTA), have been developed and are considered as important diagnostic tools for identifying patients with CAD, especially symptomatic patients [3]. CCTA is not a gold standard method for the diagnosis of CAD, however, it is a useful tool for determining the best management for patients with CAD [4]. In addition to its advantages, CCTA has some limitations, including exposure to high doses of radiation and low sensitivity and specificity due to blooming artifacts caused mainly by the calcification of vessels [5].

Another non-invasive and commonly used technique is the coronary artery calcium score (CACS). CACS is considered to be a well-established and validated imaging tool. The available evidence indicates that it could have clinical applications in both symptomatic and asymptomatic patients [6,7].

CACS in asymptomatic patients could be used as a prognostic tool for CAD diagnosis, independent of traditional risk factors [8]. In symptomatic patients, the association between CACS and CAD has a high sensitivity but low specificity, and there are reports claiming that the absence of coronary artery calcification cannot definitely rule out stenosis [9].

The association between CACS and CAD, its related future cardiac events and mortality has been investigated previously in several studies [10–12].There are also some studies evaluating the prognostic value of CACS for determining the presence and severity of CAD [13,14]. There are controversies regarding the usefulness of CACS for predicting coronary artery stenosis. Some studies reported that the usefulness of CACS is limited in some age groups or high-risk populations, and recommended to use CCTA instead [15].

It is also suggested that, given the fact that the occurrence of CAD, its related risk factors and different presentations in various ethnic populations [16], the predicting value of the score would not be similar in different populations.

Given the increasing trend for CAD morbidity [1] and the necessity of early detection in order to prevent its complication as well as to reduce the burden of the disease, and the presence of controversies regarding the usefulness of CACS for predicting coronary artery stenosis, the aim of this study was to determine the prognostic value of CACS for evaluating the presence and severity of CAD in patients with sign and symptoms of the disease. Our results could provide useful information on early detection of high-risk patients using this non-invasive method.

Material and Methods

In this cross-sectional study, all consecutive patients with suspected CAD referred to the radiology department of Alzahra hospital, affiliated to Isfahan University of Medical Sciences, for coronary computed tomography angiography (CCTA) were enrolled. This study was conducted from September 2015 to March 2016.

The protocol of this study was reviewed by the radiology department review board and the ethics committee of Isfahan University of Medical Sciences and approved with a research project number of 293416.

During this study, medical files and radiological findings of the patients were reviewed. Patients with a history of percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG), coronary stenting or previous myocardial infarction/acute coronary syndrome were excluded.

Multidetector CT technique

A 64-slice MDCT scanner (LightSpeed VCT 64, GE Healthcare, USA) was used.

First, for the purpose of calcium scoring, an area from the tracheal carina down to the diaphragm was scanned without contrast with a slice thickness of 3 mm, tube voltage of 100 or 120 kV(considering patients mass index) and tube current of 300 mA. Secondly, a contrast-enhanced, retrospective ECG-gated technique was used for a coronary study. The scan delay was calculated by the test bolus technique using 15 ml of non-iodinated contrast agent and then a bolus of 85 ml of the contrast,followed by 40ml of saline injected intravenously at a flow rate of 5 ml/second via the antecubital vein. The coronary CT angiography examination parameters were as follows: collimation, 64×0.625 mm; tube voltage, 120 kV; tube current, 400–600 mA; tube rotation time, 350 ms; pitch of 0.2. The images were initially reconstructed at 75% of the R-R interval but other phases were used if needed.

Multidetector CT image analysis

The Agatston method (by smart score software) was used for the quantification of the calcium score. The left main, left anterior descending, left circumflex and right coronary arteries (RCA) were examined for the presence of calcified plaques in the non-contrast axial slices and a total score was recorded. Source images and semi-automatically traced images of coronary arteries were evaluated by a radiologist using dedicated software (Advantag Windows 4.3, GE Healthcare). The presence of plaque and severity of stenosis were determined at the maximal stenotic site and compared to the proximal and distal sites. Different severities of coronary artery stenosis based on the CCTA report were classified into five groups as follows: 1) no plaque, 2) non-significant plaque, 3) significant stenosis in a single vessel, 4) significant stenosis in two vessels, 5)significant stenosis in three vessels. The mean CACS was determined in each group of patients with different severities of coronary artery stenosis and compared between groups. The association between CACS and different CAD risk factors was determined as well. Different cutoff points of CACS with the highest sensitivity and specificity for discriminating between different levels of coronary artery stenosis were determined.

Statistical analysis

All recorded data were analyzed using the SPSS software (V.20, SPSS Inc., Chicago, USA). The mean (SD) CACS in different groups of coronary artery stenosis was compared using the t-Student test. The association between CACS and different severities of coronary artery stenosis was determined using the Spearman test. Specificity and sensitivity of different cutoff points for CACS for discriminating between different levels of coronary artery stenosis was determined using receiver operating characteristic (ROC) curves.

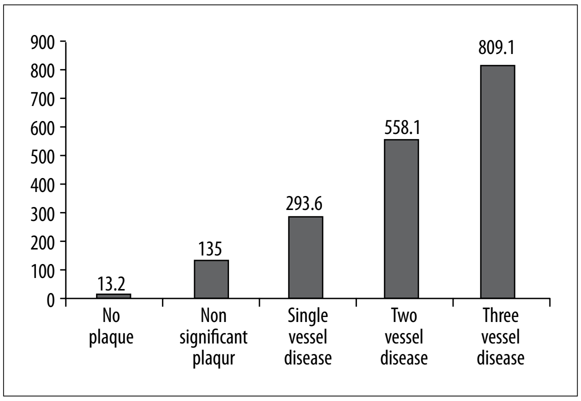

Figure 1. Mean coronary artery calcium score (CACS) in patients with different severity of coronary artery disease (CAD) determined by coornary CT angiography (CCTA).

Results

In this study, medical files of 748 patients [390 (52.1%) male and 358(47.9%) female] with suspected CAD and referred for CCTA were reviewed. The mean (SD) age of the studied population was 53.96 (12.1) years. The frequency of patients with no plaque, non-significant plaque, single-vessel disease, two-vessel disease and three-vessel disease was 54.4%, 19%, 14%, 7.4% and 5.2%, respectively.

The mean CACSs in patients with different severities of coronary artery stenosis are presented in Figure 1. The mean CACS increased significantly with increasing severity of the coronary vessel stenosis ($P<0.0001$).

The Spearman correlation coefficients indicated that there was a significant positive association between the severity of CAD and CACS ($P<0.001$, $r=0.781$).The results of ROC curve analysis for discriminating CAD (presence of stenosis) from the non-stenosis condition, non-significant stenosis from those with different grades of significant stenosis, single-vessel stenosis from two-vessel stenosis and two-vessel stenosis from three-vessel stenosis are presented in Figure 2.

ROC curve analysis indicated that the optimal cutoff point for discriminating CAD (presence of stenosis) from the non-stenosis condition was 5.35 with 88.6% sensitivity and 86.2% specificity. Predictive positive and negative values for this cutoff point were 84.4% and 90%, respectively. Area under the curve for discriminating CAD (presence of stenosis) from the non-stenosis condition was 92.1% (Figure 2A).

The optimal cutoff point for discriminating non-significant stenoses from those with different grades of significant stenosis was 106.5, with 70.4% sensitivity and 68.3% specificity. Predictive positive and negative values for this cutoff point were 75.7% and 62.2%, respectively. Area under the curve for discriminating non-significant stenoses from those with different grades of significant stenosis was 73.1% (Figure 2B).

The optimal cutoff point for discriminating single-vessel stenosis from two-vessel stenosis was 255.5, with 70%sensitivity and 63% specificity(Figure 2C). The optimal cutoff point for discriminating two-vessel stenosis from three-vessel stenosis was 410.5, with 59% sensitivity and 68.3% specificity. Predictive positive and negative values for this cutoff point were 75.7% and 54.5%, respectively(Figure 2D).

Area under the curve for different levels of coronary artery stenosis did not have sufficient sensitivity and specificity for discriminating between different levels of CAD severity (<70%).

Discussion

In this study, we compared CACS in different grades of coronary artery stenosis determined by CCTA and evaluated different cutoff levels for CACS for discriminating between different levels of coronary artery stenosis. Our results indicated that CACS is associated with the severity of coronary artery stenosis. ROC curve analysis showed that the cutoff of 5.33 for CACS had appropriate sensitivity and specificity for discriminating "no plaque" from the non-stenotic condition. However, other cutoffs determined for the differentiation between different grades of stenosis had insufficient sensitivity and specificity for predicting coronary artery stenotic severity. The cutoff determined for discriminating significant from non-significant stenoses, though acceptable (>70%), had insufficient sensitivity and specificity.

As mentioned above, the results of different studies regarding the usefulness of CACS for predicting coronary artery stenosis are not conclusive [10–14]. Some authors suggested that it could be a good predicting factor for mild to moderate stenosis [13]. Others have reported that it has insufficient predictive value [14]. Overall, there were great controversies in this regard. The results of two different studies from our region were not similar either [13,14]. Thus, we aimed to evaluate the usefulness of this score for predicting CAD, its severity and CAD-related risk factors in our population.

The results of the Multi-Ethnic Study of Atherosclerosis (MESA) cohort indicated that CACS has a better predictive value for CAD than traditional risk factors [8].

Yamamoto et al. investigated the clinical applications of CACS in identifying high-risk Japanese patients. They indicated that higher CACS values are associated with an increased risk of CAD and its related mortality. They concluded that in spite of having appropriate clinical value for both symptomatic and non-symptomatic patients, higher CACS values have insufficient accuracy [7].

In a study in Taiwan, Liu et al. evaluated the prognostic value of CACS for CAD and cardiac events based on 5 years of follow-up. They reported that CACS had a significant association with the presence of CAD and its related cardiac events in a vessel-based study. They showed that with increasing CACS, the involvement of coronary vessels is greater. They concluded that this score could be used as an additional filter before CCTA among symptomatic patients, but we should consider also the fact that the presence of significant CAD could not be excluded by CACS equal to zero [17].

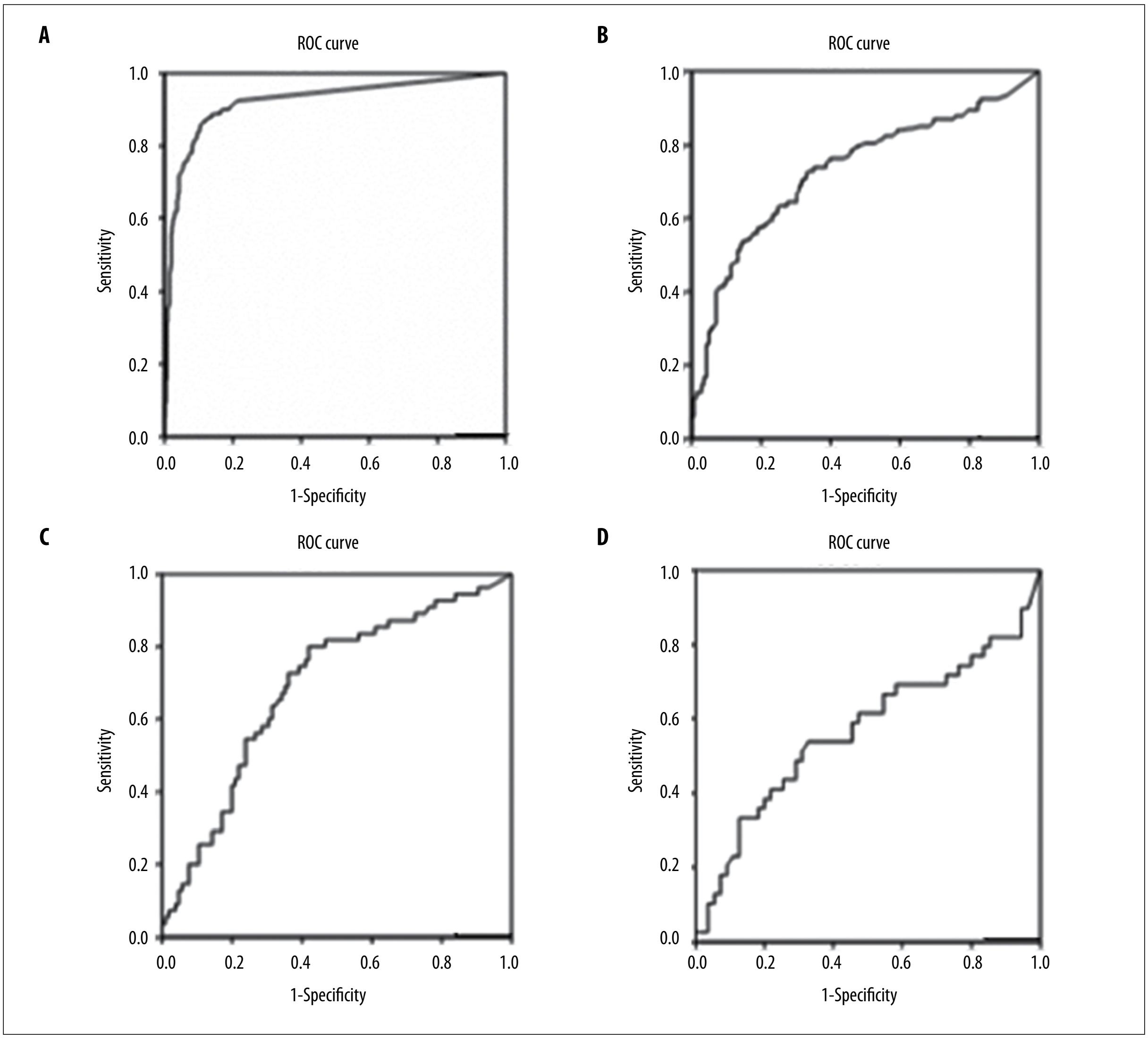

Figure 2. ROC curve analysis for discriminating CAD (presence of stenosis) from non stenoosis condition (**A**), non significant stenosis from those with different grade of significant stenosis (**B**), single vessel stenosis from two vessel stenosis (**C**) and two vessel steosis from three vessel stenosis (**D**).

Similarly, many studies indicated that in spite of the fact that a higher score of CACS is associated with a higher risk of CAD, there is no conclusive agreement with respect to low or zero CACS s and the occurrence or severity of CAD. Results of current documents in this field indicated that occurrence of CAD in each population is based on the lower cutoff level of CACS [18]. The results of different studies are not similar. Some authors reported a cutoff level of 100 for CACS, whereas others reported a cutoff level of 10.The recommendations in different guidelines are not similar as well [16,19–20].

The results of two recent regional studies were not similar either [13,14]. Almasi et al. evaluated the value of CACS for predicting the presence and severity of CAD among 202 patients. Their findings confirmed the association between CACS and CAD occurrence as well as its severity. They reported a cutoff value of 350 for CACS for predicating coronary artery involvement. They concluded that this score could be used as an additional filter prior to CCTA among suspected patients, especially those with mild to moderate CAD risk factors [13].

Motevalli et al., in a study performed in Iran with a larger sample size, indicated that the presence and different grades of stenosis in CCTA are associated with CACS, but it had insufficient sensitivity for determining coronary artery stenosis. They concluded that CCTA is superior to CACS for the detection of CAD. The strength of their study was the larger sample size and also the evaluation of vessel-specific CACS as prognostic factors for the occurrence of CAD. According to their vessel-specific CACS findings, the left anterior descending artery(LAD) calcium score had appropriate specificity for ruling out stenosis and the left main (LM) calcium score had appropriate sensitivity for diagnosing stenosis [14].

In our study, the sample size was not as large as that of Motovalli and colleagues, but was higher than that of Almasi et al. Our results regarding the association between

CACS and the presence and severity of CAD were similar to the both above-mentioned studies. In this study, we determined a cutoff value of 5.3 for distinguishing stenosis of coronary artery from the non-stenosis condition and a cutoff value of 106.5 for the differentiation between non-significant stenosis and different grades of significant stenosis. The values are lower than those reported by Almasi et al. We did not find any appropriate cutoff value for the discrimination between different grades of stenosis.

Considering our findings, it is suggested that CACS could be used as a screening score for diagnosing coronary artery stenosis, but further evaluation of CAD severity should be performed by CCTA.

Gitsioudis et al., in Germany, studied the usefulness of CACS as a filter scan before CCTA for the detection of CAD based on age, gender and CAD risk factors. Their results showed that CACS should be limited to younger patients, especially women with an intermediate risk profile in order to prevent the unnecessary exposure to radiation and CCTA is recommended in this group of patients [15].

Thus, considering the finding of the above-mentioned study, we could also recommend CACS as a screening tool that could be used in mild to moderate risk patients, and in high-risk patients CCTA is a preferable diagnostic method.

A limitation of the current study was its cross-sectional and retrospective design. Moreover, we did not evaluate vessel-specific CACS.

Conclusions

We demonstrated that there is a significant association between CACS and the presence as well as the severity of CAD. CACS could have an appropriate prognostic value for the determination of coronary artery stenosis but not for discriminating between different severities of stenosis.

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