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ORIGINAL ARTICLE

Predictive and prognostic value of 256-slice computed tomography angiography in patients with suspected coronary artery diseases

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ABSTRACT

Background: Coronary computed tomography angiography (CCTA) is commonly used to diagnose coronary artery diseases (CADs). We aimed to determine the utility of CCTA among patients suspected with CAD at the Prince Sultan Cardiac Center Qassim. **Materials and Methods:** CCTA results of 425 cardiac patients, complaining of chest pain with suspected CAD, were used to classify coronary artery stenosis into two types: obstructive if the luminal stenosis was ≥50% or nonobstructive if it was <50%. Follow-ups were conducted through clinic or phone-based interviews to document any of the following endpoints: nonfatal myocardial infarctions (MIs) or cardiac deaths (CDs), representing the major cardiac events. All other cardiac cases, including hospitalization with unstable angina, and/or late coronary revascularization, were documented. **Results:** Patients with a normal coronary artery were 278 (65.5%). The number of patients with nonobstructive and obstructive diseases was 85 (20%) and 62 (14.5%), respectively. After 19.6 ± 7 months of follow-up, 21 cardiac events occurred in twenty patients: five major adverse events (two CDs and three nonfatal MIs), ten hospitalizations due to unstable angina, and six late coronary revascularizations. Furthermore, the cumulative all-cardiac-event rates in patients with normal coronary arteries, nonobstructive CAD, and obstructive CAD were 3 (1%), 7 (8.2%), and 11 (17.7%), respectively. However, patients with normal CCTA had no major cardiac events during the follow-up. **Conclusion:** CCTA can provide valuable prognostic information on patients with suspected CAD. Patients are likely to have excellent intermediate outcomes if the coronary arteries are confirmed to be normal by CCTA.

Key words: Angiography, coronary artery, prognosis

INTRODUCTION

Cardiovascular diseases are the leading causes of deaths worldwide, and coronary artery diseases (CADs) are the most common among them. Although the currently available management of CAD is effective in reducing cardiac deaths (CDs),[1] early disease detection and identification of patients at risk, with subsequent application of proper preventive measures, is considered a more efficient method for reducing cardiovascular events.[2,3] Coronary computed tomography angiography (CCTA), a noninvasive tool for ruling out CAD, enables a comprehensive assessment of the coronary tree,[4] including lesion severity, extent, and atherosclerotic plaque components.[5] CCTA can be used

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for stratification of individuals with suspected ischemic heart diseases.[5-8] Multiple studies discuss the value of prognostication using CCTA, especially in patients with CAD. However, no similar studies have been conducted in Saudi Arabia. Therefore, we sought to investigate the prognosis of CAD using CCTA in patients with chest pain.

MATERIALS AND METHODS

Patient selection

The study recruited 425 consecutive patients with chief complaints of chest pain, who were suspected to have CAD. Between December 2012 and April 2016, all patients were referred for CCTA either from the outpatient clinic or enrolled during hospital admission. For this study, basic demographic variables, clinical data, family history of cardiovascular diseases, indications for CCTA, and follow-ups were obtained by a trained researcher blinded to the CCTA data, either using medical records or telephone interviews.

A total of 80 patients, 59 patients who were lost during the follow-up after CCTA, 12 patients who had only non-enhanced computed tomography (CT) done for calcium score, and 9 patients who had noninterpretable CCTA results due to the presence of artifacts, were excluded from the study. We obtained institutional ethical approval for the study before the conduction. The study was conducted in accordance with the Declaration of Helsinki.

Coronary computed tomography angiography acquisition

All CCTA was performed using 256-slice CCTA (Siemens Definition Flash®, Siemens Healthcare, Forchheim, Germany). CCTA data were acquired while the patients held their breath during deep inspiration. We used beta-blockers before the scan to keep heart rate <65 beats/min. A test bolus technique, using 15 ml of contrast agent, was flushed with a 30 ml saline, at a flow rate of 5 ml/s. Next, an injection of 80 ml contrast agent, followed by a 50 ml saline flush, at a flow rate of 5 ml/s, was administered for CCTA.

Coronary computed tomography angiography data analysis

The Agatston method was used to assess the coronary calcium score. Then, the CCTA scans were reviewed by experienced cardiologists using commercially available software (Syngo, Multimodality Workplace, Siemens AG, Forchheim, Germany). The coronary arteries were divided into 16 segments as follows: 1 – left main coronary artery; 2 – proximal; 3 – mid; 4 – distal left anterior descending artery; 5 – proximal; 6 – mid; 7 – distal diagonal branch; 8 – proximal; 9 – mid; 10 – distal left circumflex coronary artery; 11 – proximal; 12 – mid; 13 – distal obtuse marginal branch; 14 – proximal; 15 – mid; and 16 – distal segments of the right coronary artery.[9]

Visual estimation was used to quantify the coronary lesions. Each segment was assessed by the maximum stenosis severity and graded based on the recommendation of the Society of Cardiovascular Computed Tomography as follows: minimal, mild, moderate, and severe, with luminal stenosis of 1%–24%, 25%–49%, 50%–69%, and ≥70%, respectively.[10] In our study, any stenosis of more than 50% was considered obstructive CAD.

Clinical follow-up

The incidence of hard cardiac events was followed up in all patients, including CDs and/or nonfatal myocardial infarctions (MI). In addition, all cardiac events were recorded, including hard cardiac events, late coronary revascularization, and/or hospitalization for unstable angina. All documented deaths were considered cardiac in origin unless noncardiac causes were established. Late revascularization was defined as any coronary revascularization procedure carried out more than 90 days after CCTA. Nonfatal MI was defined as the existence of ischemic-like chest pain, typical electrocardiogram changes, and elevated cardiac enzymes.

Statistical analysis

The mean ± standard deviation was used to describe the quantitative data, whereas the categorical data were described as percentages. We used the two-sample Student's *t*-test to analyze the normally distributed data, whereas the Chi-square test was used for association when required. We assessed the cumulative event-free survival rates over the follow-up period using the Kaplan–Meier method. Patients were categorized based on the vessel involvement as follows: single-vessel disease (1-VD), 2-VD, and 3-VD. Consequently, the survival curves of all cardiac events were compared using the log-rank test. $P < 0.05$ was considered statistically significant and our level of significance was set at 0.90. All the data were analyzed by SPSS version 19.0 (SPSS Inc., Chicago, Illinois, USA).

RESULTS

Baseline characteristics

A total of 425 patients completed the study in a median of 20 months (13.5–26.6 months). Among them, 262 (61.5%) were male with a mean age of 49 ± 12 years. The indications for CCTA were chest pain in 365 (86%) patients, shortness of breath in 51 (12%) patients, and abnormal stress test in 9 (2%) patients. The baseline characteristics are shown in Table 1.

Cardiac computed tomography angiography

We found through CCTA that normal coronary arteries existed in 278 (65.5%) patients, whereas 85 (20%) patients had nonobstructive CAD with <50% stenosis, and 62 (14.5%) patients had obstructive CAD with ≥50% luminal stenosis. Other CCTA findings are shown in Table 1.

Survival analysis

During the follow-up period, 21 cardiac events occurred in twenty patients: two CDs, three nonfatal MIs, ten cases of hospitalization due to unstable angina, and six cases of late coronary revascularizations. The cumulative number of cardiac events was as follows: 3 (1%) in patients with normal CCTA, 7 (8.2%) in patients with nonobstructive CAD, and 11 (17.7%) in patients with obstructive CAD.

Furthermore, we found that patients with cardiac events were significantly older (51 ± 14 vs. 49 ± 12 years, $P = 0.047$) and mostly men (19 (90)% vs. 244 (60%), $P = 0.028$). These patients tended to have significantly higher calcium scores when compared to patients with no documented cardiac events (115 ± 170 vs. 18 ± 69 HU, $P \leq 0.0001$), respectively [Table 2].

Table 1: Baseline characteristics

Age (years), mean±SD	49±12
Male sex, *n* (%)	262 (61.5)
Body mass index (kg/m^2), mean±SD	30.6±5.4
Diabetes mellitus, n (%)	121 (28.5)
Hypertension, *n* (%)	181 (42.6)
Dyslipidemia, *n* (%)	37 (8.7)
Family history of CAD, *n* (%)	8 (2)
Current smoking, *n* (%)	44 (10.4)
Cholesterol (mmol/l), mean±SD	4.1±1.5
LDL (mmol/l), mean±SD	2.7±1.2
HDL (mmol/l), mean±SD	1.2±0.31
CT data	
Calcium score mean (minimum–maximum)	22 (0–1537)
Normal coronary arteries, *n* (%)	278 (65.5)
Nonobstructive CAD, *n* (%)	85 (20)
Obstructive CAD, *n* (%)	62 (14.5)
1-VD, *n* (%)	34 (8.0)
2-VD, *n* (%)	12 (2.8)
3-VD or significant left mean disease	16 (3.7)
CAD stenosis ≥70%	36 (8.5)

CAD: Coronary artery disease, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, VD: Vessel disease, CT: Computed tomography, SD: Standard deviation

In Kaplan–Meier curves, and during the median 20-month follow-up, the cumulative all event-free survival rates were 98.9% in patients with normal CCTA versus 88.4% in patients with a coronary stenosis of any severity [Figure 1]. In addition, we found that patients with nonobstructive CAD have a significantly higher rate of all event-free survival when compared to obstructive CAD (96.5% vs. 77.4%, $P < 0.0001$) [Figure 1]. Furthermore, the cumulative free-survival rates were significantly higher with an increased number of affected coronary arteries (82.4% with 1-VD, 83.3% with 2-VD, and 62.5% with 3-VD [$P < 0.0001$]).

More importantly, major cardiac events were not reported when coronary arteries were normal. Univariate logistic regression showed that age, male sex, a coronary calcium score >0, and the existence of luminal coronary stenosis were independent predictors of cardiac events. Moreover, multivariate regression, adjusted to age and gender, showed that 3-VD and obstructive CAD were also independent predictors of cardiac events [Table 3].

DISCUSSION

In this study, we found that noninvasive coronary imaging using CCTA can provide valuable prognostic information on symptomatic patients, with suspected CAD. Importantly, patients with normal CCTA had an excellent prognosis without any major cardiac events at the 20-month follow-up. Conversely, the majority of documented cardiac events occurred in patients with coronary stenosis of 50% or more, particularly in those with 3-VD.

CCTA in coronary stenosis is a reliable tool with an excellent negative predictive value. In addition, it can

Table 2: Clinical characteristics of the patients with and without clinical outcomes

Variables	Patients without events	Patients with events	*P*
Number of patients (%)	405 (95.3)	20 (4.7)	
Sex men (%)	244 (60)	18 (90)	0.028
Age (years), mean±SD	49±12	51±14	0.047
Diabetes mellitus, *n* (%)	112 (28)	9 (45)	0.093
Hypertension, *n* (%)	170 (42)	11 (55)	0.25
Dyslipidemia, *n* (%)	35 (8.6)	2 (10)	0.66
Family history of coronary artery disease, *n* (%)	7 (2)	1 (5)	0.54
Current smoking, *n* (%)	40 (10)	4 (20)	0.15
Calcium score, mean±SD	18±69	115±170	<0.0001
Any coronary stenosis	130 (32)	17 (85)	<0.0001
Coronary stenosis ≥50%, *n* (%)	48 (12)	14 (70)	<0.0001

SD: Standard deviation

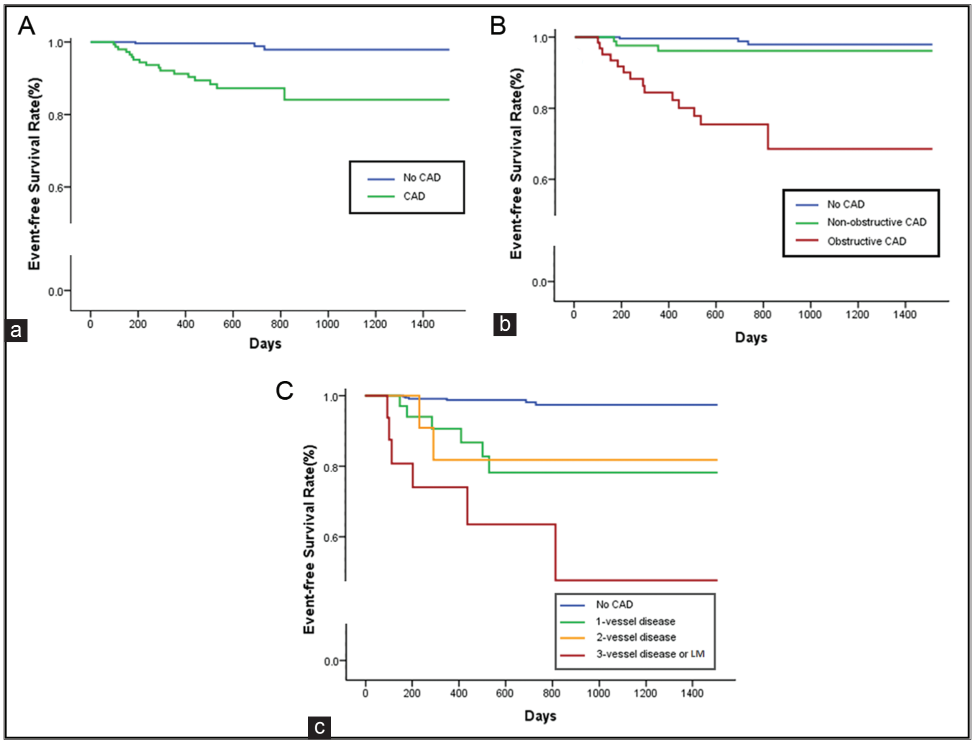

Figure 1: Survival curves for (a) normal coronary arteries and coronary artery disease. (b) Nonobstructive coronary artery disease and obstructive coronary artery disease. (c) Numbers of vessels with obstructive coronary artery disease. The numbers in each figure represent the 22-month event-free survival rates

Table 3: Univariate and multivariate analyses of coronary artery diseases risk factors and coronary computed tomography angiography variables for cardiac events, corrected for clinical risk factors

Variable	Unadjusted HR (95% CI)	*P*	Adjusted[a] HR (95% CI)	*P*
Any coronary stenosis	12.048 (3.448–41.666)	<0.0001	2.501 (0.473–13.157)	0.28
Any obstructive coronary ≥50% stenosis	17.354 (6.367–47.301)	<0.0001	5.847 (1.443–23.809)	0.013
Three-vessel obstructive CAD	16.949 (5.405–52.631)	<0.0001	2.673 (1.587–7.397)	0.018
Calcium score >0	1.003 (1.000–1.006)	0.025		
Age (years)	1.045 (1.005–1.087)	0.029	1.027 (0.982–1.074)	0.24
Male	5.939 (1.395–25.941)	0.018	6.225 (1.289–30.062)	0.023
Diabetes	0.467 (0.189–1.158)	0.1		
Hypertension	0.592 (0.240–1.460)	0.25		
Family history	7.053 (0.700–71.014)	0.29		
Smoking	0.438 (0.140–1.375)	0.15		
Dyslipidemia	0.346 (0.074–1.630)	0.18		

[a]Analysis adjusted for age and sex. SD: Standard deviation, CAD: Coronary artery disease, HR: Hazard ratio, CI: Confidence interval

provide a comprehensive evaluation of the extent and types of atherosclerotic plaque[4] and can help in planning the revascularization procedure.[11,12] Multiple studies showed that CCTA could precisely predict adverse cardiovascular outcomes and the combined endpoint, including all-cause mortality. Of particular interest, the study by Andreini *et al.*[13] demonstrated that normal CCTA has an excellent prognostic value with very low annual event rate at 52-month follow-up. Furthermore, CONFIRM (COronary CT Angiography EvaluatioN For Clinical Outcomes: An InteRnational Multicenter) registry, showed that both plaque burden and a stenosis of more than 50%, particularly in any proximal segment, carry an incremental prognostic value for CCTA in predicting the cardiac events.[14] Moreover, Hou *et al.*[15] found that the 3-year cumulative cardiovascular events increase with an increasing number of stenosed vessels.

Our findings support the result of the previous reports, which showed that obstructive CAD is well associated with increased cardiovascular events at the 20-month follow-up, and in contrast to previous reports, only a 256-slice machine was used to perform CCTAs in our analysis.

Our study has several limitations. First, the number of cardiac events was small. Second, the median follow-up was 20 months; hence, long-term follow-up is required in the future. Third, our study utilized a single center for analysis; therefore, multicenter studies with larger numbers of patients should be conducted.

CONCLUSION

CCTA provided incremental prognostic information on individuals with suspected CAD. Adverse cardiovascular events are extremely low with normal CCTA at the 20-month follow-up.

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Conflicts of interest

There are no conflicts of interest.

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