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Characteristics and clinical impact of coronary computed tomography angiography following exercise stress testing for evaluating coronary artery disease

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Abstract

Exercise stress testing (EST) remains effective in assessing coronary artery disease (CAD), especially in developing countries, while coronary computed tomography angiography (CCTA) is being increasingly utilized. However, limited data exist on whether CCTA following EST can affect diagnosis or treatment. This study aimed to characterize patients who underwent CCTA following EST and evaluate its clinical impact. Consecutive patients who underwent CCTA after EST for CAD assessment between 2014 and 2021 were included in the study. CCTA results were categorized as obstructive CAD, nonobstructive CAD, and normal. Clinical and EST characteristics were compared among groups. Multivariable logistic regression analysis was used to identify independent predictors of obstructive CAD. The diagnostic impact and therapeutic consequences of CCTA were assessed at the subsequent clinic visits. A total of 209 patients (64% male, age 60 ± 10 years) with 26% known CAD were included. The most common indication for CCTA was an inconclusive EST (31%). CCTA revealed obstructive CAD in 53 patients, nonobstructive CAD in 111 patients, and normal results in 45 patients. Multivariable analysis identified hyperlipidemia (odds ratio 3.60, 95% confidence interval 1.27–10.22, $P = .01$) and the Duke Treadmill Score (odds ratio 0.86, 95% confidence interval 0.80–0.92, $P < .001$) as independent predictors of obstructive CAD. CCTA had a diagnostic impact on 69% of all patients (76% for patients with no known CAD and 50% for patients with known CAD), including the exclusion of obstructive CAD in patients with a positive EST; the diagnosis of obstructive CAD, nonobstructive CAD, or normal CCTA in patients with an inconclusive EST; and the diagnosis of both obstructive and nonobstructive CAD in patients with a negative EST. Therapeutically, CCTA led to medication changes in 38% of patients, while 24% underwent invasive procedures. In conclusion, among patients undergoing CCTA following EST for CAD assessment, hyperlipidemia and the Duke Treadmill Score were identified as independent predictors of obstructive CAD. CCTA also had significant diagnostic and therapeutic impacts in this population.

Abbreviations: CAC = coronary artery calcium score, CAD = coronary artery disease, CAG = coronary angiography, CCTA = coronary computed tomography angiography, CI = confidence interval, ECG = electrocardiography, EST = exercise stress test, IQR = interquartile range, OR = odds ratio.

Keywords: clinical impact, coronary artery disease, coronary computed tomography angiography exercise stress test, treadmill stress testing

1. Introduction

Coronary artery disease (CAD) is one of the leading causes of morbidity and mortality worldwide.[1] Assessing the pretest probability of CAD is crucial for selecting the most appropriate diagnostic test. Exercise stress testing (EST) is a non-invasive, safe, and affordable method for diagnosing and

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The datasets generated during and/or analyzed during the current study are not publicly available, but are available from the corresponding author on reasonable request.

The study protocol was approved by the Siriraj Institutional Review Board (SIRB) (COA no. Si 416/2024). The Ethics Committee waived the requirement for written informed consent for participation due to the retrospective design of the study. All procedures involving human data were performed in accordance with the Declaration of Helsinki. The authors are accountable for all aspects of the work, ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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stratifying the risk of CAD in patients with intermediate pre-test probability.[2] Furthermore, patients with good exercise capacity and negative EST results demonstrated a favorable prognosis.[3]

Although EST offers several benefits, its sensitivity of 60% to 70% and specificity of 70% to 80% may not be excellent compared to modern imaging modalities such as stress myocardial perfusion imaging or stress magnetic resonance imaging.[4] Additionally, EST has limited diagnostic accuracy in patients postcoronary revascularization,[2] and a proportion of patients may demonstrate nondiagnostic or equivocal EST results due to inadequate exercise or other factors, such as subtle electrocardiographic changes.[5,6] Coronary computed tomography angiography (CCTA) has emerged as a modality of choice in patients with suspected CAD, as recommended in recent guidelines.[7,8] The benefits of CCTA include providing high-resolution images, the ability to characterize plaque morphology, and accurately define the degree of coronary stenosis.

However, in developing countries, including Thailand, CCTA may not be available in all areas, and EST remains an initial test. It is valuable to note that some patients may benefit from undergoing CCTA following EST, especially those with inconclusive EST results. Studies have shown that CCTA may provide additional benefits for this group of patients.[9,10] Nevertheless, there is limited data regarding the impact of CCTA following EST on diagnosis or patient management, including changes in medication for enhanced risk reduction or further invasive procedures. We aimed to characterize patients who underwent CCTA following EST and evaluate its clinical impact.

2. Methods

2.1. Study population

This retrospective cohort study included consecutive patients aged 18 years or older who underwent CCTA within 6 months of an EST for CAD assessment at the Division of Cardiology, Department of Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand, between 2014 and 2021. Patients were excluded if they had incomplete EST or CCTA information, or if they did not have follow-up data after CCTA. Information on baseline demographic variables was obtained from electronic medical records. Known CAD (prior EST) was defined using (i) history of myocardial infarction, (ii) abnormal stress test, (iii) presence of significant CAD on coronary angiography (CAG; >70% stenosis of 3 vessels or > 50% stenosis of the left main coronary artery), and (iv) history of coronary revascularization, including percutaneous coronary intervention or coronary artery bypass grafting. A history of hypertension, diabetes mellitus, hyperlipidemia, and stroke was defined according to recent guidelines.[7,11–13] Electrocardiography (ECG) was obtained on the date of the EST, and laboratory results were retrieved from the medical records within 3 months of the EST. The study protocol was approved by the Siriraj Institutional Review Board (COA no. Si 416/2024). The Ethics Committee waived the requirement for written informed consent for participation due to the retrospective design of the study.

2.2. Exercise stress testing[2]

EST was performed using a Marquette Case 8000 system (GE Medical Systems) according to the American College of Cardiology and American Heart Association practice guidelines, employing the standard Bruce protocol.[2] Continuous monitoring of blood pressure, heart rate, and ECG was conducted for up to 5 minutes into recovery. Exercise time was defined as the duration from the start of the exercise protocol to exercise cessation. Exercise-induced angina was documented when the patient reported chest tightness during the exercise. Overall results were categorized as positive, negative, or inconclusive.[2,5,14] Positive EST was defined as the appearance of ≥ 0.1 mV horizontal or down-sloping ST-segment depression 60 to 80 ms from the J-point during exercise. Negative EST was defined as reaching a submaximal heart rate (85% of the expected rate for age) without ischemia. The result was defined as inconclusive if the test was negative but not submaximal, or if there were changes in the ST segment that did not meet positive criteria (depression > 0.5 mV but < 1 mV without angina). Recorded data included exercise time, maximal heart rate, maximal blood pressure, rate-pressure product, diagnostic changes in the ST segment, and the Duke Treadmill Score.

2.3. Coronary computed tomography angiography[15,16]

CCTA scans were conducted using a 256-slice scanner (SOMATOM Definition Flash; Siemens Healthcare, Erlangen, Germany) in accordance with established guidelines[15,16] and the institutional protocol. For patients with a heart rate above 65 beats per minute, an oral beta blocker was administered 1 h before the scan to lower the heart rate. Additionally, a sublingual dose of 0.3 mg nitroglycerin was administered before starting CCTA. Prior to CCTA, a non-enhanced, prospective ECG-gated sequential scan was performed to calculate the coronary artery calcium (CAC) score. The scan parameters were as previously described.[16] Analysis of CAC and CCTA images were performed following the standard protocol on a separate workstation (Syngovia; Siemens Healthineers, Erlangen, Germany). CAC scans were interpreted using the Agatston method.[17] CCTA scans were interpreted by visual inspection with a two-observer consensus as previously published.[16]

2.4. Clinical impact of CCTA

Two cardiologists reviewed patient information, including changes in diagnosis and management following CCTA. They independently assessed the clinical impact of each CCTA by reviewing electronic medical records up until the next outpatient visit with the ordering provider. The diagnostic impact and therapeutic consequences – including the initiation, discontinuation, or adjustment of medications, as well as the need for invasive procedures – were evaluated in all patients.

2.5. Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics for Windows version 20.0 (IBM Corp., Armonk, NY). Continuous variables with a normal distribution were presented as mean ± standard deviation, and continuous variables with a non-normal distribution were presented as median and interquartile range (IQR). The normality of the distribution of variables was examined using the Kolmogorov–Smirnov test. Categorical variables were presented as absolute numbers and percentages. Normally distributed continuous data from multiple groups were compared using one-way analysis of variance. Non-normally distributed continuous data from multiple groups were compared using the Kruskal–Wallis test. Multiple comparisons were performed using Scheffé's method. Continuous variables between 2 groups were compared using Student unpaired *t*-test or Mann–Whitney *U* test. Categorical data were compared using the chi-square test or Fisher exact test, as appropriate. To analyze the predictors of obstructive CAD, a logistic regression analysis was performed to assess univariable predictors derived from baseline characteristics and EST. Variables with a *P*-value < .05 in the univariable analysis were included in the multivariable analysis. The odds ratios (ORs) and 95% confidence intervals (CIs) were calculated, with a *P*-value < .05 considered statistically significant.

3. Results

3.1. Patient characteristics

A total of 209 patients were included in the study. The clinical characteristics of the study population are summarized in Table 1. The mean age was 60.5 ± 10.5 years, with 134 (64.1%) were male. 50 patients (23.9%) had diabetes mellitus, and 56 (26.8%) had known CAD. The most common symptom reported was atypical angina, which was presented in 56 patients (26.8%). Common indications for CCTA included inconclusive EST (65 patients; 31.1%), persistent symptoms (49 patients; 23.4%), suspected false positive EST (27 patients; 12.9%), and high cardiovascular risk (12 patients; 5.7%).

Patients were categorized into 3 groups based on CCTA findings: 53 patients with obstructive CAD (including those with known CAD and significant coronary artery stenosis on CCTA), 111 with nonobstructive CAD (including those with known CAD but no significant stenosis on CCTA), and 45 with normal CCTA findings, without plaque or stenosis (Table 1). Patients with obstructive CAD were predominantly male, had a higher prevalence of CAD risk factors, and were more likely to present with typical angina than those with nonobstructive CAD or normal CCTA. Patients with obstructive CAD were also more frequently prescribed aspirin, nitrate, and statins.

3.2. EST and CCTA characteristics

Table 2 demonstrates the EST and CCTA characteristics of the patients categorized according to their CCTA findings. The mean exercise time in the total population was 6.5 ± 2.4 minutes. The EST results were positive in 65 patients (31.1%), negative in 79 patients (37.8%), and inconclusive in 65 patients (31.1%). Among patients with obstructive CAD, 1-vessel CAD

Table 1

Clinical characteristics of the study population categorized by obstructive CAD, nonobstructive CAD, and normal, as determined by CCTA.

	Total	Obstructive CAD	Nonobstructive CAD	Normal	
	(n = 209)	(n = 53)	(n = 111)	(n = 45)	*P*-value
Age, y	60.5 ± 10.5	62.1 ± 8.8	62.9 ± 8.1	52.76 ± 13.6	***<.001****,‡
Male	134 (64.1)	41 (77.4)	73 (65.8)	20 (44.4)	***.003****,‡
CAD risk factors					
Hypertension	132 (63.2)	39 (73.6)	76 (68.5)	17 (37.8)	***<.001****,‡
Diabetes mellitus	50 (23.9)	20 (37.7)	23 (20.7)	7 (15.6)	***.02****,†,‡
Hyperlipidemia	158 (75.6)	48 (90.6)	85 (76.6)	25 (55.6)	***<.001****,†,‡
Family history of CAD	8 (3.8)	3 (5.7)	4 (3.6)	1 (2.2)	.67
Cigarette smoking	16 (7.7)	8 (15.1)	5 (4.5)	3 (6.7)	.06
Medical history					
Known CAD	56 (26.8)	17 (32.1)	39 (35.1)	0 (0)	***<.001****,‡
Ischemic stroke	8 (3.8)	3 (5.7)	2 (1.8)	3 (6.7)	.26
Heart failure	2 (1.0)	2 (3.8)	0 (0)	0 (0)	.05
Atrial fibrillation	5 (2.4)	0 (0)	2 (1.8)	3 (6.7)	.08
Symptoms					
Typical angina	9 (4.3)	6 (11.3)	1 (0.9)	2 (4.4)	***.01***†
Atypical angina	56 (26.8)	16 (30.2)	24 (21.6)	16 (35.6)	.17
Non-angina chest pain	20 (9.6)	5 (9.4)	9 (8.1)	6 (13.3)	.60
Dyspnea	54 (25.8)	13 (24.5)	29 (26.1)	12 (26.7)	.97
Other symptoms	14 (6.7)	2 (3.8)	8 (7.2)	4 (8.9)	.57
Medications					
Aspirin	94 (45.0)	33 (62.3)	51 (45.9)	10 (22.2)	***<.001****,‡
$P2Y_{12}$ inhibitors	39 (18.7)	10 (18.9)	25 (22.5)	4 (8.9)	.14
ACEIs or ARBs	70 (33.5)	24 (45.3)	35 (31.5)	11 (24.4)	.08
Beta-blockers	73 (34.9)	18 (34.0)	46 (41.4)	9 (20.0)	***.04***‡
Calcium channel blockers	54 (25.8)	13 (24.5)	33 (29.7)	8 (17.8)	.29
Nitrate	30 (14.4)	14 (26.4)	13 (11.7)	3 (6.7)	***.01****
Statin	131 (62.7)	41 (77.4)	71 (64.0)	19 (42.2)	***.001****,‡
Oral hypoglycemic drugs	34 (16.3)	14 (26.4)	15 (13.5)	5 (11.1)	.06
Insulin	4 (1.9)	2 (3.8)	2 (1.8)	0 (0)	.39
Laboratory results					
eGFR	75.9 ± 17.6	71.6 ± 16.2	74.0 ± 16.6	84.6 ± 18.5	***.001****,‡
Fasting plasma glucose	112.0 ± 24.2	115.8 ± 31.3	108.7 ± 18.4	116.3 ± 27.9	.35
HbA1c	6.6 ± 1.6	7.2 ± 2.4	6.4 ± 1.4	6.3 ± 1.1	.17
Total cholesterol	174.6 ± 39.3	172.2 ± 43.1	172.1 ± 36.6	185.5 ± 41.3	.43
Triglyceride	125.8 ± 59.2	127.1 ± 58.9	129.3 ± 63.3	111.4 ± 44.0	.55
HDL-cholesterol	53.1 ± 14.1	48.9 ± 12.5	52.1 ± 13.0	62.4 ± 16.3	***.004****,‡
LDL-cholesterol	97.8 ± 33.4	95.6 ± 34.2	95.0 ± 27.5	109.3 ± 44.6	.22
12-lead ECG					
Q waves	13 (6.2)	5 (9.4)	5 (4.5)	3 (6.7)	.47
Left ventricular hypertrophy	14 (6.7)	4 (7.5)	9 (8.1)	1 (2.2)	.35

Values are numbers (percentages) or mean ± standard deviation.

Bold-italic values are < .05.

ACEIs = angiotensin-converting enzyme inhibitors, ARBs = angiotensin receptor blockers, CAD = coronary artery disease, CCTA = coronary computed tomography angiography, ECG = electrocardiography, eGFR = estimated glomerular filtration rate, HDL = high-density lipoprotein, LDL = low-density lipoprotein.

*Obstructive CAD versus normal.

†Obstructive versus nonobstructive CAD.

‡Nonobstructive CAD versus normal.

Table 2

EST and CCTA characteristics of patients categorized by obstructive CAD, nonobstructive CAD, and normal.

	Total (n = 209)	Obstructive CAD (n = 53)	Nonobstructive CAD (n = 111)	Normal (n = 45)	*P*-value
EST					
Exercise time, min	6.5 ± 2.4	6.2 ± 2.4	6.4 ± 2.3	6.8 ± 2.7	.42
Angina during exercise	14 (6.7)	8 (15.1)	3 (2.7)	3 (6.7)	***.01****,†
Resting HR	77.7 ± 12.8	78.0 ± 11.9	75.3 ± 11.6	83.2 ± 15.0	***.002****,‡
Resting SBP	134.3 ± 17.8	136.3 ± 18.5	137.7 ± 16.5	123.8 ± 16.2	***<.001****,‡
Resting DBP	79.0 ± 10.4	79.3 ± 10.1	80.8 ± 10.4	74.3 ± 9.2	***.002****,‡
Maximum HR	137.9 ± 20.6	133.1 ± 16.4	135.3 ± 20.7	150 ± 20.4	***<.001****,‡
Maximum SBP	187.7 ± 27.7	185.6 ± 25.2	191.8 ± 28.9	180.2 ± 26.2	***<.001***‡
Maximum DBP	80.0 ± 13.9	82.1 ± 13.5	80.2 ± 14.2	76.9 ± 13.7	***.02****,‡
Rate pressure product	24,489 ± 6103	23,424 ± 5649	24,803 ± 6061	24,977 ± 6683	0.34
Median maximal ST depression, mm	0 (0, 1.4)	1.2 (0, 1.8)	0 (0, 1.0)	0 (0, 1.0)	***<.001****,†
Maximal ST depression ≥ 1 mm	78 (37.3)	33 (62.2)	30 (27.0)	15 (33.3)	***<.001****,†
Duke Treadmill Score					
Median, IQR	3.4 (−0.7, 7.0)	−1.0 (−3.9, 4.5)	5.0 (1.6, 7.5)	4.4 (1.7, 6.9)	***.004****,†
Score < 5	117 (56.0)	40 (75.5)	54 (47.7)	23 (51.1)	***.004****,†
Overall EST results					***.008****,†
Positive	65 (31.1)	23 (43.4)	28 (25.2)	14 (31.1)	
Negative	79 (37.8)	9 (17.0)	50 (45.0)	20 (44.4)	
Inconclusive	65 (31.1)	21 (39.6)	33 (29.7)	11 (24.4)	
CCTA					
Median CAC score	39.1 (0, 236.5)	225 (85.6, 410.8)	104.6 (15.9, 310.0)	0 (0, 0)	***<.001****,†
1-vessel obstructive CAD	31 (14.8)	31 (58.6)	0 (0)	0 (0)	***<.001****,†
2-vessel obstructive CAD	11 (5.3)	11 (20.7)	0 (0)	0 (0)	***<.001****,†
3-vessel or LM obstructive CAD	11 (5.3)	11 (20.7)	0 (0)	0 (0)	***<.001****,†

Values are numbers (percentages), mean ± standard deviation, or median and interquartile range.

Bold-italic values are < .05.

CAC = coronary calcium score, CAD = coronary artery disease, CCTA = coronary computed tomography angiography, DBP = diastolic blood pressure, EST = exercise stress test, HR = heart rate, LM = left main, SBP = systolic blood pressure.

*Obstructive CAD versus normal.

†Obstructive versus nonobstructive CAD.

‡Nonobstructive CAD versus normal.

was observed in 31 (14.8%), 2-vessel CAD in 11 (5.3%), and 3-vessel CAD/left main disease in 11 (5.3%).

Patients with obstructive CAD had more angina during exercise (15.1%) than those with nonobstructive CAD (2.7%) and normal CCTA (6.7%), with a significant difference ($P = .01$). Patients with obstructive CAD had a higher median maximal ST depression and a higher prevalence of patients with maximal ST depression ≥ 1 mm than those with nonobstructive CAD or normal CCTA. The median maximal ST depression was 1.2 mm (IQR 0, 1.8) for obstructive CAD, 0 mm (IQR 0, 1.0) for nonobstructive CAD, and 0 mm (IQR 0, 1.0) for normal CCTA ($P < .001$). Patients with obstructive CAD also demonstrated significantly lower Duke Treadmill Scores and a higher prevalence of patients with Duke Treadmill Scores < 5 than those with nonobstructive CAD or normal CCTA. The median Duke Treadmill Score was −1.0 (IQR −3.9, 4.5) for obstructive CAD, 5.0 (IQR 1.6, 7.5) for nonobstructive CAD, and 4.4 (IQR 1.7, 6.9) for normal CCTA ($P < .001$).

3.3. Predictors of obstructive CAD

Table 3 presents the results of the univariable and multivariable analyses of predictors of obstructive CAD. Univariable analysis revealed that male sex (OR 2.32, 95% CI 1.13–4.75, $P = .02$), diabetes mellitus (OR 2.55, 95% CI 1.29–5.04, $P = .007$), hyperlipidemia (OR 4.02, 95% CI 1.50–10.73, $P = .006$), cigarette smoking (OR 3.29, 95% CI 1.17–9.26, $P = .02$), typical angina (OR 6.51, 95% CI 1.57–27.04, $P = .01$), angina during exercise (OR 4.44, 95% CI 1.47–13.48, $P = .008$), maximal ST depression (OR 2.17, 95% CI 1.51–3.11, $P < .001$), and the Duke Treadmill Score (OR 0.86, 95% CI 0.81–0.92, $P < .001$) were significantly associated with obstructive CAD. Additionally, a positive EST was positively associated with obstructive CAD (OR 2.08, 95% CI 1.09–3.98, $P = .02$), whereas a negative EST was negatively associated with obstructive CAD (OR 0.25, 95% CI 0.11–0.55, $P < .001$). To avoid the potential for overfitting due to the relatively limited number of patients with obstructive CAD, only the 5 most significant predictors from the univariable analysis were included in the multivariable analysis. These predictors were diabetes mellitus, hyperlipidemia, maximal ST depression, the Duke Treadmill Score, and a negative EST. Multivariable analysis identified hyperlipidemia (OR 3.60, 95% CI 1.27–10.22, $P = .01$) and the Duke Treadmill Score (OR 0.86, 95% CI 0.80–0.92, $P < .001$) as independent predictors of obstructive CAD.

3.4. Diagnostic impact and therapeutic consequences of CCTA

Figure 1 and Table 4 illustrate the diagnostic impact and therapeutic consequences of CCTA, respectively. CCTA had a diagnostic impact in 145 out of 209 patients (69.4%). For patients with no known CAD, CCTA had a diagnostic impact in 117 of 153 (76.5%), and for patients with known CAD, it had a diagnostic impact in 28 of 56 (50.0%). The diagnostic impact included the exclusion of obstructive CAD in patients with a positive EST; the diagnosis of obstructive CAD, nonobstructive CAD, or normal CCTA in patients with an inconclusive EST; and the diagnosis of both obstructive and nonobstructive CAD in patients with a negative EST, as detailed in Figure 1 and Table 4.

For therapeutic consequences, CCTA led to a change in medication in 38.3% (80/209) of patients, including the addition of a new medication or an increase in the dose of current medication

Table 3

Predictors of obstructive CAD.

	Univariable analysis		Multivariable analysis	
	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
Age, y	1.02 (0.99, 1.06)	.20		
Male	2.32 (1.13, 4.75)	***.02***		
Hypertension	1.89 (0.95, 3.76)	.07		
Diabetes mellitus*	2.55 (1.29, 5.04)	***.007***	1.95 (0.93, 4.06)	.07
Hyperlipidemia*	4.02 (1.50, 10.73)	***.006***	3.60 (1.27, 10.22)	***.01***
Family history of CAD	1.81 (0.42, 7.85)	.42		
Cigarette smoking	3.29 (1.17, 9.26)	***.02***		
Known CAD	1.42 (0.72, 2.80)	.31		
Ischemic stroke	1.81 (0.42, 7.86)	.42		
Typical angina	6.51 (1.57, 27.04)	***.01***		
Atypical angina	1.25 (0.63, 2.50)	.51		
Non-angina chest pain	0.98 (0.34, 2.84)	.97		
Dyspnea	0.91 (0.44, 1.87)	.80		
Other symptoms	0.47 (0.10, 2.18)	.33		
eGFR	0.98 (0.96, 1.002)	.07		
Fasting plasma glucose	1.009 (0.99, 1.03)	.32		
HbA1c	1.30 (0.97, 1.75)	.08		
Total cholesterol	0.99 (0.98, 1.009)	.71		
Triglyceride	1.001 (0.99, 1.008)	.88		
HDL-cholesterol	0.97 (0.93, 1.002)	.06		
LDL-cholesterol	0.99 (0.98, 1.009)	.62		
Q waves on ECG	1.99 (0.61, 6.43)	.25		
Left ventricular hypertrophy on ECG	1.22 (0.36, 4.10)	.74		
EST characteristics				
Exercise time, min	0.94 (0.82, 1.07)	.32		
Angina during exercise	4.44 (1.47, 13.48)	***.008***		
Resting HR	1.003 (0.98, 1.03)	.81		
Resting SBP	1.008 (0.99, 1.03)	.34		
Resting DBP	1.003 (0.97, 1.03)	.82		
Maximum HR	0.99 (0.97, 1.00)	.05		
Maximum SBP	0.99 (0.99, 1.01)	.51		
Maximum DBP	1.02 (0.99, 1.04)	.19		
Maximal ST depression, mm*	2.17 (1.51, 3.11)	***<.001***	1.07 (0.51, 2.26)	.84
METs	0.95 (0.83, 1.08)	.43		
Duke Treadmill Score*	0.86 (0.81, 0.92)	***<.001***	0.86 (0.80, 0.92)	***<.001***
Overall EST results				
Positive EST	2.08 (1.09, 3.98)	***.02***		
Inconclusive EST	0.60 (0.30, 1.15)	.12		
Negative EST*	0.25 (0.11, 0.55)	***.001***	0.54 (0.21, 1.40)	.20

Bold-italic values are < .05.

ACEIs = angiotensin-converting enzyme inhibitors, ARBs = angiotensin receptor blockers, CAD = coronary artery disease, CCTA = coronary computed tomography angiography, DBP = diastolic blood pressure, ECG = electrocardiography, eGFR = estimated glomerular filtration rate, EST = exercise stress test, HDL = high-density lipoprotein, LDL = low-density lipoprotein, LM = left main, SBP = systolic blood pressure.

*The 5 most significant predictors from the univariable analysis that were included in the multivariable analysis were diabetes mellitus ($P = .007$), hyperlipidemia ($P = .006$), maximal ST depression ($P < .001$), the Duke Treadmill Score ($P < .001$), and a negative EST ($P = .001$).

such as antiplatelets (42/209; 20.1%) and statins (33/209; 15.8%). CCTA also led to discontinuation of antiplatelet therapy in patients with normal CCTA findings (Table 4). Additionally, 51 patients (24.4%) underwent invasive procedures after CCTA, all of whom underwent CAG. Subsequently, percutaneous coronary intervention was performed in 41 patients, whereas 10 patients underwent coronary artery bypass graft.

4. Discussion

The main findings of this study are summarized as follows: In patients who underwent CCTA after EST for CAD assessment, hyperlipidemia and the Duke Treadmill Score were independent predictors of obstructive CAD on CCTA. Additionally, CCTA had a significant clinical impact, accurately categorizing patients and influencing therapeutic decisions, including medication adjustments and the need for invasive procedures.

The diagnosis and risk stratification of patients with CAD are crucial for optimizing treatment and improving outcomes. EST is a noninvasive, safe, and affordable screening test for CAD, provided there is careful patient selection for better predictive value, especially in patients with intermediate pretest probability for obstructive CAD.[2,3,14] The majority of the population in our study had no known CAD, and the characteristics were compatible with intermediate pretest probability (mean age 60 years; 23% with diabetes mellitus; most presented with atypical angina or dyspnea) that are appropriate for risk stratification with EST. However, the accuracy of EST is limited, with a sensitivity of 68% and a specificity of 77%.[2,4] This was also true in our results: in patients with no known CAD, one-third (Fig. 1; 16/48) of the patients with positive EST demonstrated obstructive CAD on CCTA, while 9% (Fig. 1; 5/54) of the patients with negative EST had obstructive CAD. Moreover, 51 patients had inconclusive EST results that required further investigations.

CCTA has been a robust tool for the diagnosis and risk stratification of CAD since it provides excellent spatial resolution images, can characterize plaques, and accurately quantify coronary artery stenosis.[7–9] The clinical value of CCTA after stress testing has been studied previously.[9,18] Chinnaiyan et al evaluated the correlation between stress testing (9% used EST) and CCTA results in 6198 patients with low to intermediate pretest probability undergoing invasive CAG, and found a strong correlation between CAG and CCTA findings, but not with stress test results.[18] Clinical factors that were independently associated with obstructive CAD on CAG included male sex, current smoking status, older age, hypertension, and typical angina.[18] However, studies regarding CCTA following specific EST are limited, and this issue is important in developing countries where imaging stress tests may not be available in all areas. Our study, which focused on EST, also found that EST had a limited correlation with CCTA results. Variables that were independently associated with obstructive CAD on CCTA included hyperlipidemia and the Duke Treadmill Score. Another study by Lau et al evaluated 346 patients with chest pain who underwent CCTA following EST, focusing on patients with inconclusive EST.[5] They found that obstructive CAD was present in 8%, 20%, and 29% of patients with negative, positive, and equivocal ESTs, respectively, and concluded that CCTA may be an important gatekeeper test in those with low to intermediate pretest probability of obstructive CAD.[5] The correlation between EST and CCTA results in the study by Lau et al is also similar to our findings mentioned above.

The clinical impact of CCTA has been widely studied. The SCOT-HEART landmark study investigated the effects of CCTA plus standard care versus standard care alone in patients with stable chest pain. The study found a significantly lower rate of death from CAD or nonfatal myocardial infarction at 5 years in the CCTA group compared to the standard care group.[19] This could be due to the initiation of more preventive therapies in the CCTA group. McEvoy et al evaluated the impact of CCTA screening on physician and patient behavior using a health-screening program and found that abnormal screening CCTA was predictive of increased aspirin and statin use.[20] Additionally, CCTA screening was associated with increased invasive testing, without any difference in events at 18 months.[20] Another study by Limpijankit et al evaluated the association between different treatment modalities guided by CCTA and the prevention of MACE in patients with stable CAD.[21] They found that in patients with obstructive CAD, treatment with a combination of statin and aspirin, or early revascularization, was associated with a lower rate of MACEs compared to no treatment.[21] These findings demonstrate the potential benefit of CCTA in guiding appropriate treatment to prevent cardiovascular events. CCTA provides detailed images of the coronary arteries, allowing the detection and assessment of the extent and severity of CAD.

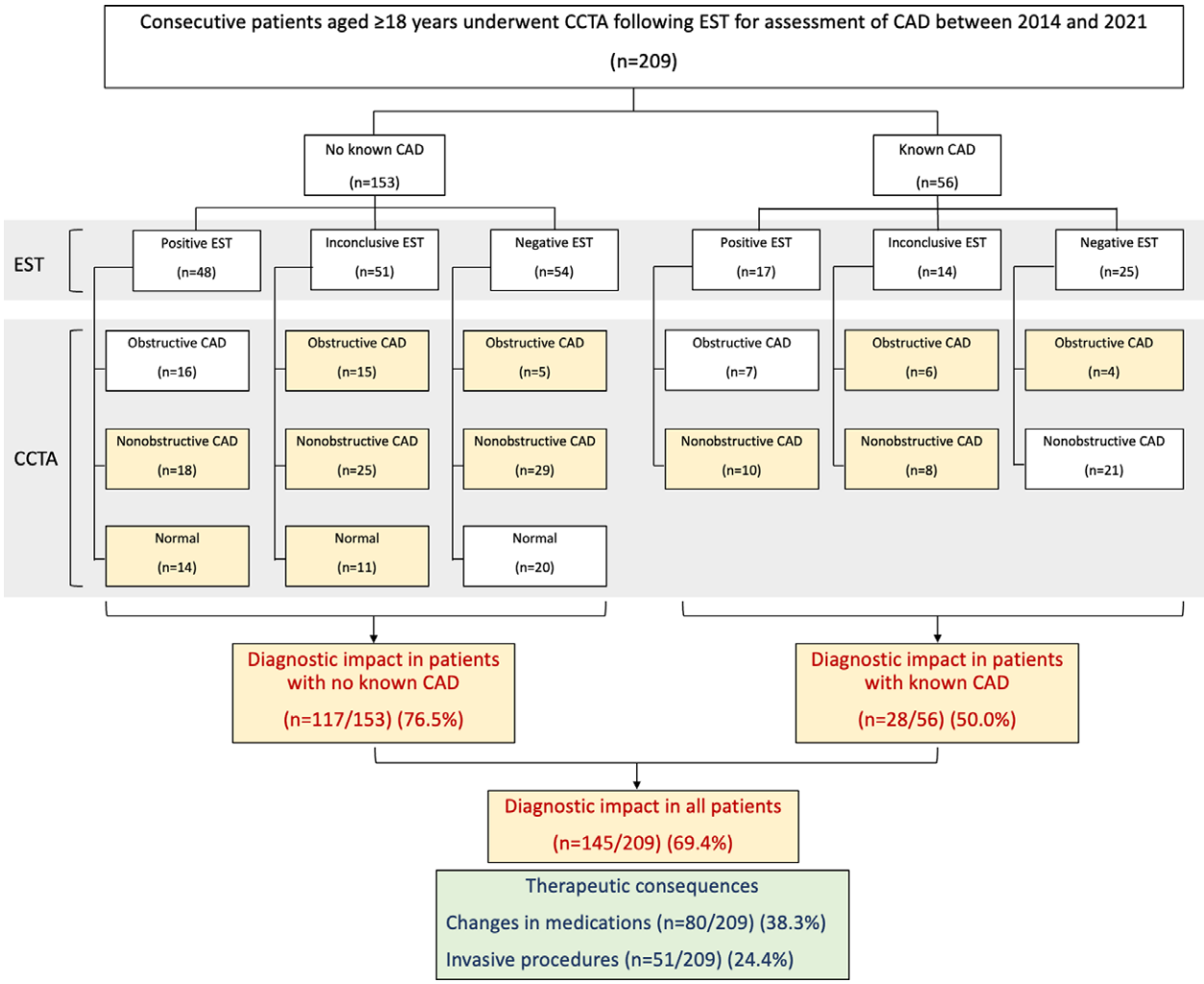

Figure 1. Diagnostic impact and therapeutic consequences of CCTA following EST. CCTA = coronary computed tomography angiography, EST = exercise stress test.

Additionally, subclinical atherosclerotic plaques identified by CAC or CCTA, even if nonobstructive, place patients in a category warranting preventive therapy.

In our study, CCTA had a diagnostic impact in nearly 70% of all patients. This included the exclusion of obstructive CAD in patients with a positive EST; the diagnosis of obstructive CAD, nonobstructive CAD, or a normal CCTA in patients with an inconclusive EST; and the identification of both obstructive and nonobstructive CAD in patients with a negative EST. Additionally, the diagnostic impact was higher for patients with no known CAD (76.5%) than for those with known CAD (50.0%). This could be explained by several factors: (1) differences in the pretest probability of obstructive CAD (or significant stenosis on CCTA) between the 2 groups, which affect the results of both EST and CCTA; and (2) patients with known CAD tended to have higher CAC scores than those with no known CAD, which also affects image interpretation (e.g., differentiating between obstructive and nonobstructive CAD).

In our study, CCTA not only had diagnostic value in reclassifying patients into obstructive, nonobstructive, or no CAD categories, but it also had a significant impact on therapeutic decisions. In patients with normal CCTA, indicating a very low risk of future cardiovascular events, antiplatelet therapy can be discontinued, especially in those with a high risk of bleeding. Patients with nonobstructive CAD or high CAC without obstructive CAD (which is often underdiagnosed by stress tests) received effective preventive therapy, such as high-intensity statins, which have demonstrated benefits in previous publications.[19,22] CCTA also served as a gatekeeper, ensuring that patients underwent appropriate invasive procedures. Overall, CCTA provided significant clinical impact in patients with prior EST in our study, highlighting the benefits of CCTA for effective preventive therapy. The clinical implications of the study include the observation that in developing countries, where EST remains a common screening tool, CCTA provides significant diagnostic and therapeutic benefits. Certain patient characteristics, including male sex, hyperlipidemia, typical angina, and the Duke Treadmill Score, were independently associated with obstructive CAD on CCTA.

5. Study limitations

This study had some noteworthy limitations. First, its retrospective design rendered it vulnerable to missing or incomplete data and certain biases. Second, there was a significant selection bias, as the study participants were limited to patients who underwent CCTA at a single institution following an EST. Importantly, not all patients who underwent EST proceeded to CCTA, as the decision to perform CCTA was influenced by clinical judgment, institutional protocols, and patient-specific factors. This selection process may have led to an overrepresentation of individuals with a higher probability of CAD, thereby affecting the generalizability of our findings. Moreover, since the

Table 4

Clinical impacts of CCTA.

Diagnostic impact	
Total number of patients with a new or changed diagnosis	145/209 (69.4%)
Patients with no known CAD	117/153 (76.5%)
Exclusion of obstructive CAD in patients with a positive EST	32/48
Diagnosis of obstructive CAD, nonobstructive CAD, and normal CCTA in patients with an inconclusive EST	51/51
Diagnosis of obstructive and nonobstructive CAD in patients with a negative EST	34/54
Patients with known CAD	28/56 (50.0%)
Exclusion of obstructive CAD in patients with a positive EST	10/17
Diagnosis of obstructive CAD, nonobstructive CAD, and normal CCTA in patients with an inconclusive EST	14/14
Diagnosis of obstructive and nonobstructive CAD in patients with a negative EST	4/25
Therapeutic consequences	
Total number of patients whose medication was changed	80/209 (38.3%)
Addition of a new medication or an increase in the dose of current medication	66/209 (32.5%)
Antiplatelets	42/209 (20.1%)
ACEIs or ARBs	9/209 (4.3%)
Beta-blockers	15/209 (7.2%)
Oral antidiabetic drugs or insulin	4/209 (1.9%)
Statins	33/209 (15.8%)
Discontinuation of medication	19/209 (9.1%)
Antiplatelets	19/209 (9.1%)
Statins	3/209 (1.4%)
Total number of patients who underwent invasive procedures	51/209 (24.4%)
Coronary angiography	51/209 (24.4%)
Percutaneous coronary intervention	35/209 (16.7%)
Coronary artery bypass graft surgery	16/209 (7.7%)

Values are numbers (percentages).
ACEIs = angiotensin-converting enzyme inhibitors, ARBs = angiotensin receptor blockers, CAD = coronary artery disease, CCTA = coronary computed tomography angiography, EST = exercise stress test.

study was conducted at a single center, the results may not be directly applicable to broader populations or different healthcare settings. Third, our study had a relatively limited sample size; nevertheless, it successfully demonstrated the diagnostic and therapeutic impact of CCTA. Fourth, not all patients underwent CAG to confirm the results of CCTA. However, the diagnostic accuracy of CCTA has been well established.

6. Conclusions

In patients undergoing CCTA following EST for CAD assessment, hyperlipidemia and the Duke Treadmill Score were identified as independent predictors of obstructive CAD. CCTA also had significant diagnostic and therapeutic impacts in this population.

Author contributions

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