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Research Article

Gender Distribution of Coronary Artery Calcium Score and Degree of Stenosis Assessed by Computed Tomography Angiography in Iraqi Patients with Chest Pain

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Abstract

Background: Sex variations in coronary artery disease (CAD) are well documented. However, sex differences in coronary artery calcium (CAC) and its role in the detection of coronary artery stenosis remain controversial. ***Objective***: To assess the impact of sex variation on coronary artery calcification and its efficacy in predicting coronary artery stenosis. ***Methods***: This is a cross-sectional observational study including 230 consecutive patients with suspected CAD (120 men and 110 women) referred for coronary computed tomography angiography (CCTA). The study analyzed sex-based differences in the sensitivity and specificity of coronary artery calcification (CAC) for detecting moderate to severe stenosis across various coronary arteries. ***Results***: The calcification scores 1-100 and 101-<400 were slightly more frequent in men (25% and 10%, respectively) than women (20.91% and 7.27%, respectively); however, the differences were not significant. For the left anterior descending artery (LAD), men showed slightly higher sensitivity and specificity (69.23% and 81.48%, respectively) than women (61.9% and 79.78%, respectively). For the left circumflex artery (LCX), men showed relatively higher sensitivity (68.75%) and lower specificity (89.42%) than women (50% and 98.81%, respectively). For the right coronary artery (RCA), women showed relatively higher sensitivity and specificity (75% and 93.4%, respectively) than men (50% and 91.82%, respectively). ***Conclusions***: While the CAC has a relatively high specificity and low sensitivity in the detection of coronary artery disease, there is no difference in the score between men and women. When comparing vessels, women exhibit greater RCA calcification sensitivity and specificity than men, whereas for LAD, the opposite is true.

Keywords: Agatston score, Coronary artery calcium, Coronary artery disease, Sex difference.

التوزيع الجنسي لدرجة الكالسيوم في الشريان التاجي ودرجة التضيق التي تم تقييمها بواسطة تصوير الأوعية المقطعي المحوسب في المرضى العراقيين الذين يعانون من آلام في الصدر

الخلاصة

الخلفية: الاختلافات الجنسية في مرض الشريان التاجي (CAD) موثقة جيدا. ومع ذلك، لا تزال الاختلافات بين الجنسين في كالسيوم الشريان التاجي (CAC) ودوره في الكشف عن تضيق الشريان التاجي مثيرة للجدل. **الهدف**: تقييم تأثير التباين الجنسي على تكلس الشريان التاجي وفعاليته في التنبؤ بتضيق الشريان التاجي. **الطريقة**: هذه دراسة رصدية مقطعية مستعرضة تشمل 230 مريضا متتاليا يشتبه في إصابتهم بمرض الشرايين التاجية (120 رجلا و 110 أمرأة) تمت إحالتهم إلى تصوير الأوعية المقطعي المحوسب التاجي (CCTA) وحللت الدراسة الاختلافات القائمة على الجنس في حساسية وخصوصية تكلس الشريان التاجي (CAC) للكشف عن التضيق المعتدل إلى الشديد عبر الشرايين التاجية المختلفة. **النتائج**: كانت درجات التكلس 1-100 و 101-<400 أكثر تواترا بقليل لدى الرجال (25٪ و 10٪ على التوالي) من النساء (20.91٪ و 7.27٪ على التوالي) ؛ ومع ذلك، لم تكن الاختلافات كبيرة. بالنسبة للشريان النازل الأمامي الأيسر(LAD) ، أظهر الرجال حساسية وخصوصية أعلى قليلا (69.23٪ و 81.48٪ على التوالي) من النساء (61.9٪ و 79.78٪ على التوالي). بالنسبة للشريان المحيط الأيسر (LCX) ، أظهر الرجال حساسية أعلى نسبيا (68.75٪) وخصوصية أقل (89.42٪) من النساء (50٪ و 98.81٪ على التوالي). بالنسبة للشريان التاجي الأيمن (RCA) ، أظهرت النساء حساسية وخصوصية أعلى نسبيا (75٪ و 93.4٪ على التوالي) من الرجال (50٪ و 91.82٪ على التوالي). **الاستنتاجات**: في حين أن CAC لديه خصوصية عالية نسبيا وحساسية منخفضة في الكشف عن مرض الشريان التاجي، لا يوجد فرق في النتيجة بين الرجال والنساء. عند مقارنة الأوعية، تظهر النساء حساسية وخصوصية أكبر لتكلس RCA من الرجال ، بينما بالنسبة ل LAD ، فإن العكس هو الصحيح.

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INTRODUCTION

Globally, cardiovascular disease—primarily ischemic heart disease—continues to be the primary cause of disease burden in both men and women, even though women typically present seven to ten years later [1]. This concept was thought to be related to the cardioprotective effect of estrogen by long observational studies, but randomized clinical trials disprove this effect in preventing atherosclerotic changes [2]. Many studies on sex-related variations in the incidence, severity, and prognosis of coronary artery disease (CAD) have been published in recent years. Women present with distinct chest pain symptoms more frequently than men do when they have suspected acute or chronic coronary syndrome. They also have higher cardiovascular risk profiles, but less obstructive CAD [3]. Many studies have documented the significant gender disparities in the incidence and rate of atherosclerosis development, as well as the associated morbidity and mortality linked to almost any level of vascular compromise [4]. A variety of imaging modalities are available to evaluate individuals who may be suffering from coronary ischemia, such as stress electrocardiography, myocardial perfusion imaging, single-photon emission computed tomography, positron emission tomography, coronary computed tomography (CT) angiography, and magnetic resonance imaging [5]. Coronary artery calcium (CAC) scoring, which is performed using a multi-detector CT scan, has become a widely accessible, reliable, and repeatable method of evaluating risk for major cardiovascular outcomes. For a wide range of baseline risks, CAC testing in asymptomatic populations is a financially sensible option [6]. In a non-contrast study, the Agatston technique uses total weighted lesions with a density greater than 130 HU. The calcium area is multiplied by a factor that is associated with the maximum plaque attenuation (factors 1–199 HU, 2–299 HU, 3–399 HU, and 4–400 HU) [7]. Although coronary CT angiography (CCTA) shows promise as a non-invasive alternative, invasive coronary angiography remains the gold standard for diagnosing coronary artery disease. CCTA provides a quicker and potentially more economical way to evaluate patients at intermediate risk for CAD, while also avoiding the risks associated with an invasive procedure [8]. In terms of prognosis, CCTA has the advantage of both good diagnostic sensitivities for the identification of non-significant disease and a very high negative predictive value that enables the reliable exclusion of coronary artery disease (CAD) [9]. However, many conditions limit the role of CCTA, such as blooming and streak artifacts. Significantly calcified coronary artery plaques on CCTA reduce the assessment of the coronary artery lumen, a problem that dual-energy CT angiography can resolve. This technique not only reduces radiation exposure but also lessens the effects of metallic stents and highly calcified artery artifacts [10]. Catheter angiography may be necessary for further evaluation in these situations, as CCTA may not be able to exclude the presence of significant CAD. The use of heart stents may limit the evaluation of the stent lumen, leading to artifacts resembling those from calcified plaques. Therefore, catheter angiography becomes necessary in these situations [11]. Other limiting factors include severe arrhythmias and the patient's inability to hold his breath [12]. In CT angiography, few Iraqi studies are concerned with coronary artery stenosis. A study done by Mohammed *et al*. showed how the Kurdish population tends to have coronary artery disease earlier in life and that older men displayed more aggressive coronary angiographic lesions, despite the fact that cardiovascular risk factors were concentrated in the female demographic [13]. This study aims to assess sex variation in the presence and severity of coronary artery calcification, as well as the degree of stenosis.

METHODS

Study design and setting

This is an observational analytic cross-sectional study conducted at the cardiac center of Al-Kindy Teaching Hospital. The included patients are 230 adults who complained of acute retrosternal chest pain between August 2023 and January 2024. The ethics committee at Al-Kindy College of Medicine approved the study.

Patients' preparations

Before evaluation, the patient received a few instructions, such as avoiding solid food four hours beforehand and avoiding dehydration to prevent tachycardia. The heart rate should ideally be between 60 and 65 beats per minute to enhance exam resolution. This can be obtained by prescribing B-blocker drugs (such as metoprolol tab) by the patient's physician. Patients should continue to take their cardiovascular drugs as usual [14].

Exclusion criteria

Any patient with one of the following conditions is excluded from the study: heavy coronary artery calcification (calcium score greater than 600) [15], history of previous cardiac surgery, high heart rate despite rate-lowering drugs, elevated renal indices, and history of allergy to contrast media.

Outcome measurements

Coronary CT angiography was carried out using a 64-slice CT scan (Brilliance 64: Philips Medical System Corporation, best, the Netherlands), and the tube voltage was 120 KV. For the quantification of the Agatston CAC score, the slice thickness was 2.5 mm, and then we acquired the CCTA images using a 1 mm slice thickness. The automatically launched ECG viewer enabled the continuous registration of heart rate and rhythm, as well as the computation of heart rate mean and standard deviation. Once the patient's heart rate has been successfully modulated, they are taken to the scanner suite, where they are placed in a supine position on a table to produce the first localizing images. The scan consists of two-step

measurements. In the non-contrast CT scan phase, we first obtain the calcium score (Agatston score), followed by a contrast coronary CT angiography phase that measures the internal diameter of coronary arteries. We then reconstruct the data to obtain multiplanar reformation (MPR), maximum intensity projection (MIP), and volume rendering (Figure 1).

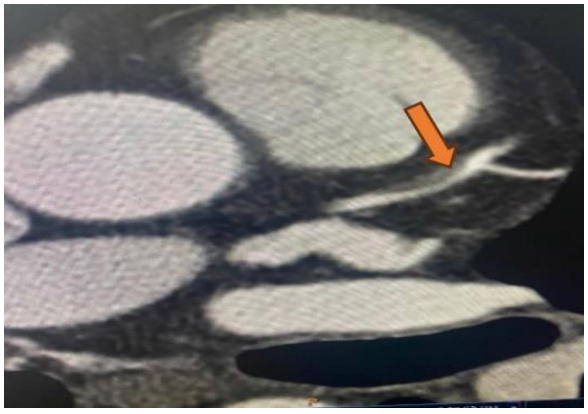

Figure 1: Coronary angiography shows non-calcified atheromatous plaque (orange arrow) involving the LAD artery causing 80 % stenosis.

It takes about 15 seconds to complete. Coronary calcium score (Agatston score) is measured using software; this software displays colored spots for calcium that are manually marked by the operator and automatically calculates all spots to a summed calcium score (Figures 2A and B).

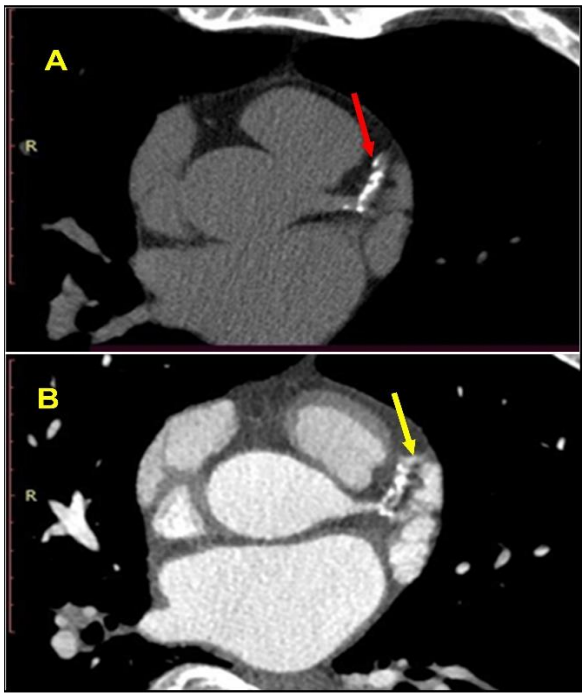

Figure 2: cardiac CT scan of a 60-year-old male who presents with acute retrosternal chest pain. A) multiple calcified plaques involving the left anterior descending artery, coronary calcium score =250 (red arrow); B) Coronary CT angiography shows more than 60% luminal stenosis (yellow arrow).

The calcified plaque is defined as a lesion consisting of at least two adjacent pixels with a density > 130 HU. The Agatston method was used by calculating the weighted sum of the lesions with a density of more than 130 HU and multiplying the area of calcification by a factor related to maximum plaque attenuation: 130-199 HU: factor 1, 200-299 HU: factor 2, 300-399 HU: factor 3, and ≥ 400 HU: factor 4 [16]. Following the injection of contrast media, specifically iopromide (Ultravist 370 mg/mL; Bayer Pharma AG, Germany), the CT angiography phase commences, and the bolus-tracking technique typically guides the scan timing for coronary CTA. With this method, a single region of interest (ROI) is often placed on the ascending aorta with a threshold value of 100 to 200 HU, and the coronary CTA scan is carried out 5-7 seconds after triggering [10]. Two radiologists with 5-year experience measure the internal diameter of coronary arteries, including the left main coronary artery, the left anterior descending artery, the left circumflex artery, the right coronary artery, and the left descending artery, to reduce bias. The CT data are reconstructed and post-processing is done in the form of multiplanar reformation (MPR), maximum intensity projection (MIP), and volume rendering. The patients were categorized into the following groups according to the results of the Agatston score: zero calcium score, calcium score > zero and < 100, calcium score ≥ 100 and < 400, and calcium score > 400. The patients were categorized into the following groups according to the results of the CT angiography: coronary artery with no stenosis, low coronary artery stenosis < 30%, intermediate coronary artery stenosis 30%–60%, and severe coronary artery stenosis > 60%.

RESULTS

This study included a total of 230 patients with suspected coronary artery diseases. Of those, 120 males (52.17%) and 110 females (47.83%). The mean age of males was 52.39±10.8 years (range 21–75 years) compared with 53.53±9.5 years (range 25–73 years) for females, with no significant difference. In either group, the majority of patients had no calcification. Although females had a higher rate of ≥ 400 scores than males (2.73% vs. 0.83%), the difference was not significant (Table 1).

Table 1: Total coronary calcium score in male and female

Categories	Male (n=120)	Female (n=110)	*p*-value
Zero	75(62.5)	77(70)	0.345
1-100	31(25.83)	22(20)	
101-<400	13(10.83)	8(7.27)	
≥400	1(0.83)	3(2.73)	

Values were expressed as numbers and percentages.

Regarding the LAD artery, the calcification scores 1-100 and 101-<400 were slightly more frequent in males (25% and 10%, respectively) than in females (20.91% and 7.27%, respectively); however, the differences were not significant (Table 2). In terms of the LCX artery, there were no scores ≥400 in either sex. Males demonstrated a non-significantly higher rate of 1-100 and 101≤400 (16.67% and 1.67%, respectively) than females (10% and 0.91%, respectively), as shown in Table 2.

Table 2: Calcium score in males and females according to each artery

Variables	Categories	Male (n=120)	Female (n=110)	*p*-value
LAD	Zero	78(65)	77(70)	0.347
	1-100	30(25)	23(20.91)	
	101≤400	12(10)	8(7.27)	
	≥400	0(0%)	2(1.82)	
LCX	Zero	98(81.67)	98(89.09)	0.284
	1-100	20(16.67)	11(10)	
	101≤400	2(1.67)	1(0.91)	
RCA	Zero	106(88.33)	100(90.91)	0.411
	1-100	13(10.83)	7(6.36)	
	101≤400	1(0.83)	2(1.82)	
	≥400	0(0.0)	1(0.91)	

Values were expressed as numbers and percentages. LAD: left anterior descending; LCX: left circumflex; RCA: right coronary artery.

However, the vast majority of either sex had no RCA calcification, and only a small minority had a 101–400 or ≥400 score, with no significant difference (Table 2). Regarding the LCX, intermediate and severe stenosis were more common in males (9.17% and 4.17%), respectively, than in females (0.91% for both), with a highly significant difference (Figure 3).

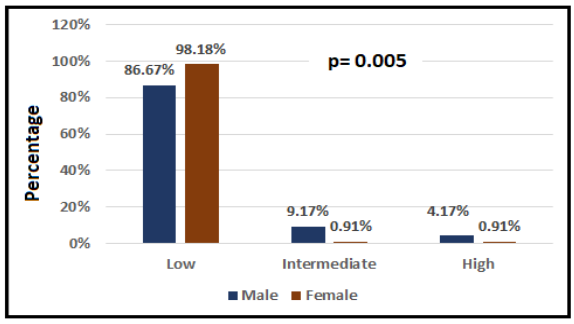

Figure 3: Degree of stenosis in LCX artery according to CT angiography in men and women.

While in the LAD artery, intermediate and severe stenosis were more common in males (20% and 12.5%, respectively) than in females (11.82% and 7.27%), but the difference was still not significant (Figure 4).

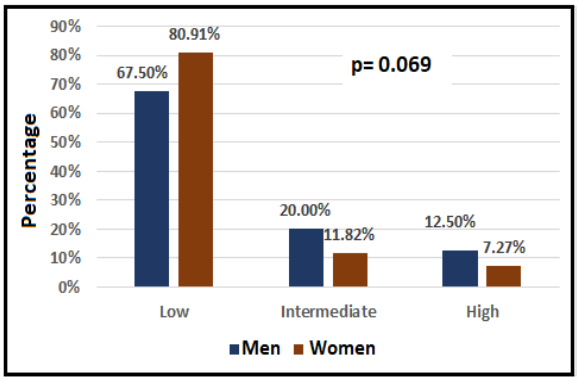

Figure 4: Degree of stenosis in LAD artery according to CT angiography in men and women.

In regards to RCA, only a minority of males and females had intermediate or severe stenosis. Both sexes had comparable degrees of stenosis, with no significant differences (Figure 5), with low stenosis being less than 30%, intermediate stenosis being between 30% and 60%, and severe stenosis being more than 60%. As shown in Table 3, males showed relatively higher sensitivity and specificity (69.23% and 81.48%, respectively) than females (61.9% and 79.78%, respectively) regarding the LAD artery, while males showed relatively much higher sensitivity (68.75%) and lower specificity (89.42%) than females (50% and 98.81%, respectively) regarding the LCX artery.

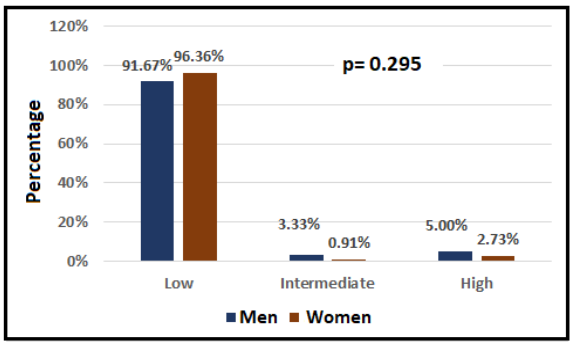

Figure 5: Degree of stenosis in RCA artery according to CT angiography in men and women.

But Females showed relatively higher sensitivity and specificity (75% and 93.4%, respectively) than males (50% and 91.82%, respectively) regarding RCA, as shown in Table 3. There was a significant positive correlation between calcification score and degree of stenosis (r= 0.471, p<0.001), as shown in Figure 6.

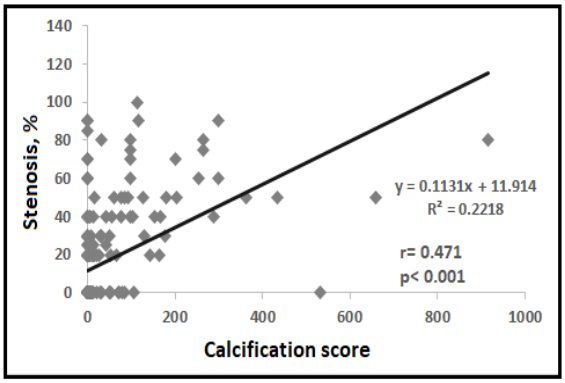

Figure 6: The correlation between coronary calcification score (CAC) and s degree of stenosis.

DISCUSSION

Ischemic coronary artery disease had a great impact on both male and female health. Multiple techniques were used to evaluate the coronary artery, like stress ECG, echocardiogram, SPECT, stress CMR, CACS, CCTA and ICA [17]. According to the result of the study, there was no significant difference between males and females regarding coronary artery calcification, either collectively (for the three coronary arteries) or individually. These results contrast with the findings of many previous studies. Raggi *et al*. examined 10,377 asymptomatic Americans, revealing that women generally exhibited lower CAC scores compared to men, particularly in cohorts with scores exceeding 400 and 1000 (p<0.0001) [18]. Similarly, Lessmann *et al*. studied

5718 Dutch patients undergoing CTA, finding a higher prevalence and severity of CAC in men (81% vs. 60%), while women displayed comparable CAC levels to men a decade younger [19].

Table 3: Comparison of sensitivity and specificity of RCA calcium score in detention of stenosis between male and female

			Men			Women		
			CTA		Total	CTA		Total
			Intermediate-High stenosis	Low stenosis		Intermediate-High stenosis	Low stenosis	
LAD		No calcification	12	66	78	8	71	79
	CAC	Calcification	27	15	42	13	18	31
		Total	39	81	120	21	89	110
	Sensitivity		69.23%			61.9%		
	Specificity		81.48%			79.78%		
			Men			Women		
			CTA		Total	CTA		Total
			Intermediate-High stenosis	Low stenosis		Intermediate-High stenosis	Low	
LCX		No calcification	5	71	98	1	97	98
	CAC	Calcification	11	18	22	1	11	12
		Total	16	89	120	2	108	110
	Sensitivity		68.75%			50%		
	Specificity		89.42%			98.81%		
			Men			Women		
			CTA		Total	CTA		Total
			Low Stenosis	Intermediate-High stenosis		Low Stenosis	Intermediate-High stenosis	
RCA		No calcification	101	5	106	99	1	100
	CAC	Calcification	9	5	14	7	3	10
		Total	110	10	120	106	4	110
	Sensitivity		50%			75%		
	Specificity		91.82%			93.4%		

McClelland *et al*. conducted a comprehensive prospective study within the Multi-Ethnic Study of Atherosclerosis (MESA), consistently showing men bearing significantly higher coronary calcium burdens across all age groups [20]. Shaw *et al*. examined calcified plaque distribution by sex and CAC subgroups, revealing that women tended to have fewer calcified lesions and vessels, with less overall calcification volume, albeit larger individual lesion sizes compared to men [21]. In a Japanese study, Nakao *et al*. demonstrated that women generally had lower CAC scores than men, with only 6.1% of women displaying scores ≥400 compared to 21.1% of men [22]. The most important factor that results in variation between the present study and previous studies is the sample size, which is small in the present study compared with other studies. In the present study, females had less intermediate and severe stenosis of the LCX and LAD coronary arteries than males, according to CTA. In line with these results, there have been several studies worldwide. A recent study by El-Mahdiui *et al*. included 211 patients who had undergone a coronary CTA for suspected CAD. At baseline, men had a higher degree of stenosis, 24.6% (14.9–33.5%) than women, 21.5% (13.3–30.8%) (p=0.044) [23]. In Australia, Chiha et al. examined 994 participants with chest pain using CTA. A vessel score was calculated based on the number of vessels with significant obstructive coronary disease. Women with chest pain scored lower on average than men did. Males were three times more likely than females to receive a positive score. Additionally, compared to men, women with chest pain had a higher likelihood of having normal coronary arteries, which could be attributed to hormonal effects, particularly estrogen [24]. In contrast, in an American study including 50 participants, 50% of whom were women, Lin *et al*. showed that women and men had a comparable prevalence of moderate or higher stenosis (36% vs. 48%). Obstructive CAD was observed at a similar frequency in both women and men (24% vs. 28%). Interestingly, all the participants in the later study were patients with type 2 diabetes, which cannot reflect the real effect of sex differences due to the variation in disease duration and glycemic controls [25]. The possible explanations for observed sex differences in moderate to severe stenosis may be attributed to the vasodilatory influence of estrogens on coronary vessels, which induces salutary changes in lipid profiles, inhibition of vascular smooth muscle cell proliferation, antioxidant activity and an anti-inflammatory effect [26]. In the present study, CAC had generally low sensitivity and very good specificity in detecting severe coronary artery stenosis. Furthermore, in the vessel-specific comparison, there was a mixed result. The test yielded better results for RCA vessels in women, but not for LAD. A Japanese study by Yamamoto et al. (2014), which investigated the clinical applications of CAC in identifying CAD among 723 patients with suspected CAD, aligns with this result. They concluded that, in spite of having appropriate clinical value for both symptomatic and non-symptomatic patients, higher CAC values have insufficient accuracy [27]. Motevalli *et al*. suggested that while CTA can identify the presence and varying degrees of stenosis associated with CAC, it lacks adequate sensitivity in determining coronary artery stenosis. Notably, their study, along with a handful of others, including ours, assessed vessel-specific CAC as a predictor of CAD. In Motevalli's findings, the LAD calcium score showed suitable specificity for excluding stenosis, while the LAD calcium score demonstrated appropriate sensitivity for diagnosing the condition [28]. In the current study, the LCX exhibited the highest sensitivity, and the RCA showed the highest specificity. Haberl *et al*. utilized receiver-operating characteristic curves to evaluate CAC's sensitivity and specificity in predicting CAD among

1,764 Dutch patients (1,225 men and 539 women), finding no significant differences in test accuracy between the gender subgroups [29]. Using CTA, Nakao et al. investigated 991 participants (456 women and 535 men) with suspected CAD and observed that incorporating CAC into a prediction model significantly enhanced CAD detection, particularly among women [22]. In another study of 1851 patients (including 682 women) with suspected CAD, Budoff *et al*. demonstrated that although diagnostic performance was similar between women and men, the specificity of CAC for detecting coronary artery stenosis was better in women than in men [30]. This variation between different studies could be explained by the variation in stenosis severity as well as the criteria for stenosis categorization. The present study has many limitations. First, there was not enough information to distinguish between atypical angina and non-anginal chest pain, which is usually critical for predicting coronary artery obstruction. Secondly, there was a lack of data to evaluate the predictive value of ECG findings. Collectively, the present study indicates that there is no significant variation in the CAC score between men and women, while CAC has relatively high specificity and low sensitivity in detecting CAD. A vessel-specific comparison indicated higher sensitivity and specificity of RCA calcification in women than men, while the reverse is true for LAD.

Limitations of the study

The present study has many limitations. First, there was not enough information to distinguish between atypical angina and non-anginal chest pain, which is usually critical for predicting coronary artery obstruction. Secondly, there was a lack of data to evaluate the predictive value of ECG findings. Another limitation is that the sample sizes are small and single-center. Therefore, we suggest conducting a study of variables other than gender, such as smoking, diabetes, and lipid profile, in a larger multi-center study with a large sample size.

Conclusion

There is no significant variation in the CAC score between men and women, while CAC has relatively high specificity and low sensitivity in the detection of coronary artery disease. Vessel-specific comparisons indicate higher sensitivity and specificity of RCA calcification in women than men, while the reverse is true for LAD.

Conflict of interests

No conflict of interests was declared by the authors.

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Data sharing statement

Supplementary data can be shared with the corresponding author upon reasonable request.

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