Iraqi JMS

Published by Al-Nahrain College of Medicine
ISSN 1681-6579
Email: iraqijms@colmed-alnahrain.edu.iq
http://www.colmed-alnahrain.edu.iq

Prevalence of Coronary Artery Disease in Symptomatic Patients with Zero Calcium Score Undergoing Coronary CT Angiography

Mohammed A. Kadhim[1] *FIBMS*, **Wassan A.K. Al-Saadi**[1] *FACMS*, **Ghassan H. Hadi**[2] *MBChB*

[1]Section of Radiology, Dept. of Surgery, College of Medicine, Al-Nahrain University, [2]Dept. Radiology, Al-Imamian Al-Kadhimian Medical City, Baghdad, Iraq

Abstract

Background Non-invasive coronary angiography is being increasingly performed by computed tomography angiography to assess obstructive coronary artery disease. There is increasing interest in the absence of coronary artery calcification, as a "negative" cardiovascular risk factor. The frequency and clinical relevance of coronary artery disease in patients without coronary artery calcification are unclear.

Objective To assess the presence and the severity of coronary artery disease in symptomatic patients without coronary artery calcification (Calcium score of zero).

Methods One hundred and ten cases (62 females and 48 males) with mean age of 50.4 years with no detection of calcified plaques in the coronary arteries (coronary artery calcification score=zero) were studied. Known or suspected cases of coronary artery disease underwent a coronary computed tomography angiography examination. Calcium score examination was conducted immediately before coronary computed tomography angiography. Degree of stenosis was found by comparing the luminal diameter of the narrowest segment of the artery with that of a more proximal or distal normal segment of the same artery.

Results Stenosis was found in 23/110 patients, giving a prevalence of (20.9%), among the 23 cases with stenosis: the right coronary artery stenosis was found in 19/23 (82.6%), left anterior descending in 11/23 (47.8%) and left circumflex artery in 5/23 (21.7%). Mean percentage of stenosis was highest in right coronary artery (59.9%). In 52.2%, only one vessel was involved, in (43.5%) two vessels were involved and in (4.3%) three vessels were involved.

Conclusion Coronary computed tomography angiography can clearly demonstrate noncalcified atherosclerotic coronary plaques in a large group of patients with suspected coronary artery disease. The absence of coronary artery calcification does not exclude the presence of significant stenosis in symptomatic patients with no coronary Calcium.

Keywords Coronary artery disease, Zero Calcium score, CT coronary angiography

List of abbreviation: CAD = coronary artery disease, CT: computed tomography, CACS = coronary artery calcium scoring, CCTA = coronary computed tomography angiography, ECG = electrocardiogram, RCA = right coronary artery, LAD = left anterior descending, LCXA = left circumflex artery.

Introduction

Coronary artery disease (CAD) is the leading cause of death in the world. Identifying new risk factors and improving the screening methods for CAD are continuously evolving processes. The presence of calcium in coronary arteries is pathogenomonic of atherosclerosis, as confirmed by histopathology and intravascular ultrasound studies [1-3]. The implementation of multidetector computed tomography (CT) at the end of the 1990s resulted in the widespread use of Coronary artery calcium scoring (CACS) [4]. The latter represents a

reliable linear anatomic estimate of total plaque burden [5]. Nearly all prospective studies have found moderate-to-high CAC to be an independent and incremental predictor of future cardiovascular events over conventional risk factors and the Framingham Risk Score [6-15]. Therefore current guidelines recommend measurement of CAC for further risk stratification of intermediate risk individuals, in whom treatment with long-term aspirin and statin therapy is most uncertain [6, 16].

Calcified plaques represent older lesions, and newer plaques are more likely to be lipid rich and poor in calcium [17]. There is increasing interest in the absence of CAC (a calcium score of 0) as a "negative" cardiovascular risk factor [18,19]. Absence of CAC might reliably exclude obstructive coronary disease in asymptomatic and selected symptomatic individuals and seems to be associated with a low cardiovascular event rate, suggesting that less aggressive pharmacotherapy might be indicated in this population [20].

However, published event rates for individuals with 0 CAC vary, likely owing to differences in baseline risk, follow-up period, as well as outcome ascertainment and verification [19]. The characteristics of the few individuals with 0 CAC who subsequently develop cardiovascular events have not been well- described. Less is known about the prognosis of a low positive CAC score (CAC 1 to 10), because most studies are underpowered to report this as a distinct group. Some studies have reported increased and variable non-calcified soft coronary plaque in patients with low CAC [21]. In patients with a CAC score <10, coronary computed tomography angiography (CCTA) provides excellent diagnostic performance with a very high specificity [22].

One concern is the presence of isolated lipid-laden (soft) plaque in the setting of a negative study (zero calcium score). The ability to detect lipid-laden coronary plaques with cardiac CT angiography would possibly improve risk stratification of these patients [23]. Recent studies found varying degrees of noncalcified plaques using coronary CT angiography in patients with a CAC score of zero [21,24,25].

CCTA has become a noninvasive diagnostic option for detecting critical coronary artery stenosis in patients with low or moderate risk [26]. and can be employed as a screening tool for selected populations in the identification of patients at higher risk for ischemic events. Those people would benefit from further testing and more aggressive risk factor modification [27]. The determination of significant stenotic disease in persons with some level of calcification will undoubtedly be useful to the clinician and patient [28].

The aim of the study is to assess the presence and the severity of CAD in symptomatic patients without coronary artery calcification (Calcuium score of zero).

Methods

A prospective cross-sectional study was employed at AL-Sader Medical City in Al- Najaf health directorate, performed from April to December 2014. A total of 110 patients (62 females, 48 males; mean age, 50.4 years [range, 21-75 years] were enrolled in the study. All the patients included in the study had no detectable calcified plaques in the coronary arteries (CAC score=zero). A known or suspected cases of CAD (patients complaining from chest pain and atypical angina) underwent a coronary CT angiography examination; Ca score examination was conducted immediately before coronary CT angiography.

The exclusion criteria were: patients with Ca score above zero, the coronary CT angiography examination was suboptimal, and the coronary arteries could not be sufficiently evaluated, history of coronary artery bypass graft and/or prior stent placement, as well as lack of sinus rhythm or history of any allergic reaction to contrast agent, renal function impairment, patient with myeloma or any patient in whom administration of contrast will be risky. Other patient-related factors that can interfere with the diagnostic quality of CTCA are irregular

heart rhythm (atrial fibrillation or frequent extra systoles) and inability to sustain a breath hold for at least 15 to 20 seconds.

The CT examination was performed in a calm and comfortable atmosphere (e.g., lights were dimmed, and the staff speaks quietly), avoiding anything that might affect the patient's heart rate, because a constant rate is crucial for image quality and diagnostic accuracy in CCTA. Patients asked to avoid anything that can increase their heart rate, such as talking during the scan or moving too much, also avoid caffeine, smoking and advice B blocker (metoprolol 50 mg) for one day before exam. CT coronary angiography was performed with a 64-slice scanner (Aquillon 64, V4.51 ER 010, Toshiba Medical Systems, Tochigi; Japan) with retrospective electrocardiogram (ECG) gating.

As soon as the patient has been placed on the table in the supine position with the arms above the head he or she should not move, in order to ensure that the planned scan region matches the region actually scanned and that the entire coronary tree is imaged. The patient should be shifted slightly to the right side of the table, so that the heart is as close to the center as possible (since spatial resolution is highest in the center of the scan field). The ECG electrodes should be placed so that they do not disturb the patient, while ensuring optimal identification of R-wave signals by the ECG monitor.

In the CCTA examination, about 80-100 ml of iodinated contrast agent (Omnipaque, 350 mg/mL iodine) was administered by dual head injector through an 18–20 G cannula, which was placed in the right antecubital vein. Then 40 ml saline was administered. The optimal scan time was determined using the automatic bolus tracking method.

Before Multi-Slice CTA, a non-contrast CT was acquired to measure calcium score according to the Agatston and volumetric methods for the whole heart (total heart calcium) as well as the individual coronary arteries [left main stem (LM), left anterior descending artery (LAD), left circumflex artery (LCX) and right coronary artery (RCA)] using sequence scan with slice thickness of 3 mm. When the patient heart rate was more than 65 bpm, a β-blocker (metoprolol 50 mg orally was administered before the scan. Breath holding exercise were done for all patient A bolus of 80 -100ml contrast medium (Omnipaque, 350 mg/mL iodine) was injected intravenously at a rate 5 ml/s, followed by 40 ml of normal saline. The scan was obtained from the aortic arch to the level of the diaphragm during a single breath hold.

With ECG triggered scanning protocol was performed, the following parameters were used: Collimation width 32.5×32.5 cm, slice thickness 0.5 mm, rotation time 0.35 s, tube voltage 120 kV, maximum effective tube current 890 mA, table feed 0.3 mm/rotation AT 75% of R-R cardiac cycle. The examination time about 10 seconds.

CT images were reconstructed using a smooth kernel (B25f) with a slice thickness of 0.5 mm (increment 0.3mm). CT data sets were transferred to dedicated workstation (VITREA 2 WORKSTATION vital image Plymouth, Minnesota, USA) for image analysis. The total calcium score of coronary arteries were calculated by Agatston and volumetric methods. To avoid observer variability, two radiologists had measured and read the calcium scoring.

The composition (calcified, noncalcified/soft, or mixed) of the plaques was established. Only the cases that had Agatston score=zero were included in the study and the patients were divided into 2 groups: with and without plaques (stenosis and without stenosis) as observed in coronary CT angiography. The degree of stenosis was assessed by comparing the lumen diameter of the narrowest segment with that of a more proximal or distal normal segment. Stenoses were classified as mild (<39% stenosis), moderate (40-69% stenosis) and severe (70-99% stenosis).

Statistical analysis

Data are presented as mean ± standard deviation or as numbers and percentages. Categorical data are expressed as frequencies and were compared with Pearson's Chi-square test. Continuous variables are presented as the mean ± standard deviation and were compared using ANOVA (analysis of variance). A probability (P) value of less than 0.05 was considered statistically significant. Data were analyzed with SPSS software version 20.

Results

There were 110 patients enrolled in this prospective study. The mean age of the studied group was 50.4 ± 9.1 (range: 21-75) years, furthermore, 17 patients (15.5%) aged ≤ 40 years, 46 patients (41.8%) aged 41-50 years, 34 patients (30.9%) aged 51-60 years and 13 patients (11.8%) aged > 60 years. Regarding the gender distribution, males were 48/110 represented (43.6%) of the studied group and females were 62/110 and represented (56.4%), with a female to male ratio of (1.3:1).

According to the CCTA findings of the studied group, stenosis of different degree was found in 23 patients (20.9%) while the remaining 87 patients (79.1%) had no stenosis.

Among the 23 patients with stenosis, right coronary Artery (RCA) stenosis was the most prevalent and found in 19 patients (82.6%), left anterior descending artery (LADA) stenosis in 11 (47.8%) and left circumflex artery (LCXA) in 5 patients (21.7%), this was statistically significantly (P = 0.015).

Further analysis revealed that mean percentage of stenosis was 59.9 ± 14.7 in RCA, 47.7 ± 12.8 in LADA and 56 ± 19.5 in LCXA, There is statistically significant difference when comparing stenosis in RCA and LADA, P value is 0.046 as shown in table 1.

Table 1. Mean stenosis percentage of the involved arteries among positive group

Artery	No.	Mean ± SD	Range	P value
RCA	19	59.9 ± 14.7	26-80	RCA vs. LADA = 0.046
LADA	11	47.7 ± 12.8	27-75	RCA vs. LCXA = 0.43
LCXA	5	56.0 ± 19.5	30-80	LADA vs. LCXA = 0.28

RCA = right coronary artery, LAD = left anterior descending, LCXA = left circumflex artery

In 12 patients (52.2%) only one vessel was involved, in 10 patients (43.5%) two vessels were involved and in one patient only (4.3%) three vessels were involved, indicated that one vessel involvement was the more frequent finding, followed by two vessels and the least frequent was the three vessels involvement, this findings was statistically significant (P = 0.011).

Mild RCA stenosis was found in 4 patients (21.1%), moderate in 9 patients (47.3%), and severe RCA stenosis was found in 6 patients (31.6%). Regarding the LADA, each of mild and moderate stenosis was found in 5 patients (45.5%), and severe stenosis was found in only one patient (9.1%). The mild LCXA stenosis was found in one patient (20%), moderate stenosis in two patients (40%), and severe in 2 patients (40%). By comparing the severity of stenosis between the three arteries, no significant differences had been found in the degrees of severity (mild, moderate and severe) between these arteries, P = > 0.05, as shown in table 2.

The prevalence of stenosis was significantly increased with advanced age, this findings was statistically significant (P = 0.015), furthermore, the mean age was significantly higher in patients with stenosis than those without; 55.5 ± 7.8 years vs. 49.1 ± 8.8 years, respectively. Regarding the association between stenosis and gender, no statistically significant difference had been found in the prevalence of stenosis between males and females, 18.8% vs. 22.6%, respectively (Table 3 and Fig. 1-3).

Table 2. Distribution of severity according to the involved vessel

Severity of stenosis	Artery						P value
	RCA (n=19)		LADA (n=11)		LCXA (n=5)		
	No.	%	No.	%	No.	%	
Mild (25 - 49%)	4	21.1	5	45.5	1	20.0	0.32
Moderate (50 - 69%)	9	47.3	5	45.5	2	40.0	0.95
Severe (70 - 99%)	6	31.6	1	9.1	2	40.0	0.29
Total	19	54.3	11	31.4	5	14.3	0.48

RCA = right coronary artery, LAD = left anterior descending, LCXA = left circumflex artery

Table 3. The age and gender distribution of the studied group with positive and negative stenosis

Parameter		Positive (N=23)		Negative (N=87)		Total	P value
		No.	%	No.	%		
Age (Years)	≤ 40	0	0.0	17	100.0	17	0.015
	41 - 50	8	17.4	38	82.6	46	
	51 - 60	9	26.5	25	73.5	34	
	> 60	6	46.2	7	53.8	13	
	mean ± SD	55.5 ± 7.8	-	49.1 ± 8.8	-	-	0.002
Gender	Male	9	18.8	39	81.2	48	0.62
	Female	14	22.6	48	77.4	62	
Total		23	20.9	87	79.1	110	

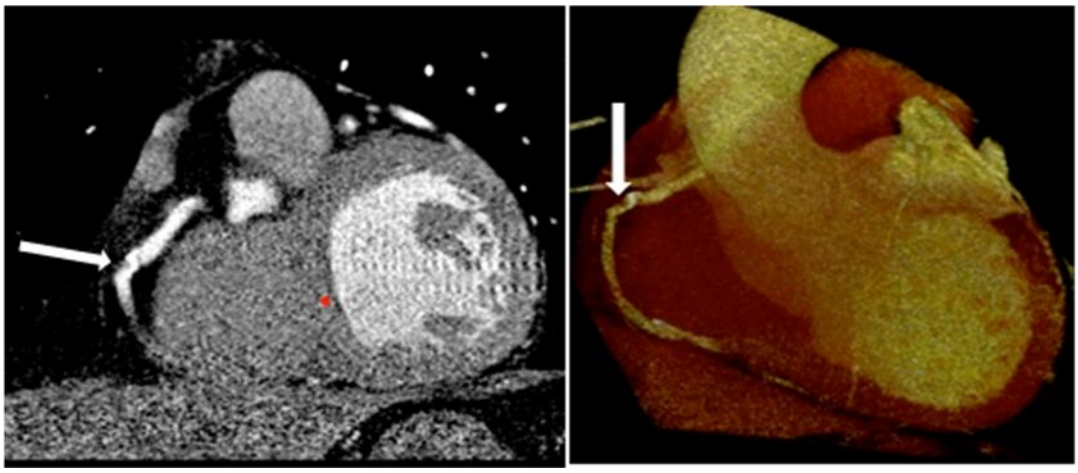

Fig. 1. 60 year-old symptomatic man. Curved planar reformatted (Left) and volume-rendered (Right) CT angiography images show a noncalcified soft plaque (*white arrows*), which is causing a significant (65%) stenosis in the RCA

Discussion

Because non calcified plaques can be found in cases of CAD in addition to calcified plaques, the CAC score examination has numerous limitations in detecting coronary atherosclerosis. Recent studies found varying degrees of noncalcified plaques using coronary CT angiography in patients with a CAC score of

zero. Acute coronary syndromes frequently result from the rupture of these noncalcified small plaques, which are generally not flow-limiting and do not cause stenosis. Calcification is a marker of plaque stability, whereas an unstable plaque is characterized by a large lipid core, a thin fibrous cap, and inflammation. An unstable plaque has been termed the "vulnerable plaque". The early detection of these plaques is important because they have a tendency to rupture but respond to medical treatment [26].

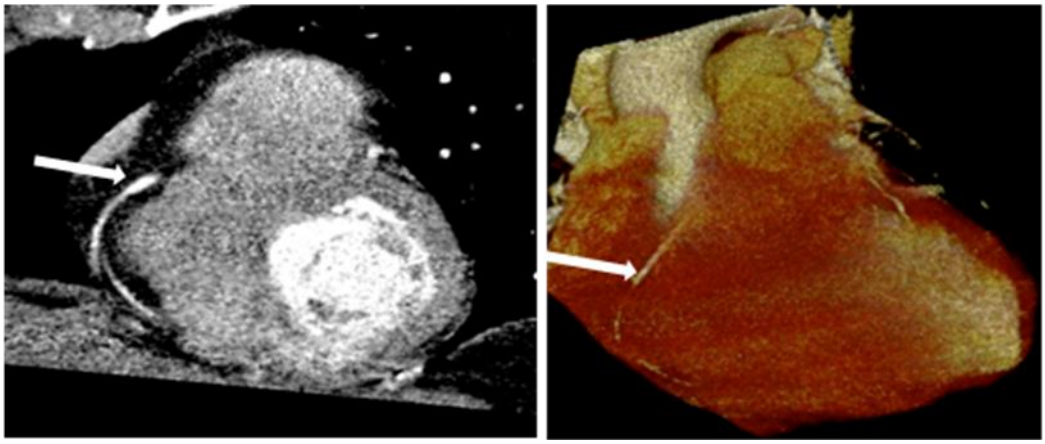

Fig. 2. A 65-year-old symptomatic woman. Curved planar reformatted (Left) and volume-rendered (Right) CT angiography images show a noncalcified soft plaque (*white arrows*), which is causing a significant (70%) stenosis in the RCA

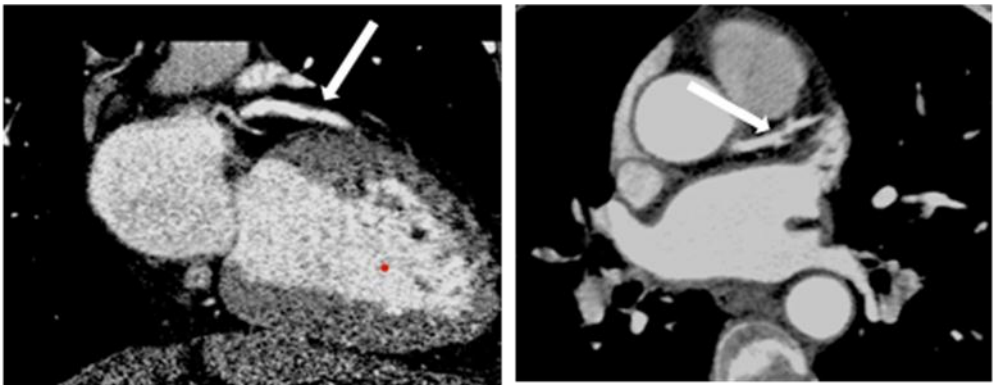

Fig. 3. A 54-year-old symptomatic woman. Curved planar reformatted (Left) and axial (Right) CT angiography images show a noncalcified soft plaque (*white arrows*), which is causing a significant (60%) stenosis in the LAD

The most important result of this study was the presence of coronary atherosclerosis at a high prevalence of 20.9% in patients with a CAC score of zero. The presence of noncalcified plaques in cases with a CAC score of zero has been reported at varying frequencies in the literature [21,25,29-31]. These rates were reported to be 6.5% by Cheng et al [21], 10% by Choi et al [29], 12% by Sosnowski et al [25], and 20% by Ergün et al [30]; however, Kelly et al. [31] reported a rate as high as 51%. These different rates may have resulted from the differences in the characteristics of the patient populations that were included in the studies.

Regarding the gender distribution, in our study, we observed that there is no significant difference between male and female gender (P value 0.62), this agreed to Kitagawa et al [32]

and Iwasaki et al [33]. On the other hand Büyükterzi et al [26] in a study Of 238 patients without plaques according to coronary CT angiography, they found that 126 (53%) were males and 112 (47%) were females, although the frequency of plaques was higher in males, this increase was not statistically significant (*P* = 0.153).

Regarding the site of stenosis we observed that among the 23 patients with stenosis, the RCA stenosis was the more prevalent it was found in 19 patients (82.6%) , LADA stenosis in 11 (47.8%) and LCXA in 5 patients (21.7%) , according to this findings, the RCA stenosis was significantly the more prevalent among the positive stenosis group, P = 0.015. Tse-Min Lu et al [34] found significant RCA disease was much more common than other arteries in their population. We also found that the mean percentage of stenosis was 59.9 ± 14.7 in RCA, 47.7 ± 12.8 in LADA and 56 ± 19.5 in LCXA with statistical significance between RCA and LAD (P value= 0.046). In Tse-Min Lu et al [34] study, they found that in a total of 164 patients included in the study 95 patients (57.9%) had significant RCA stenosis and 69 (42.1%) patients without stenosis. In patients with RCA disease, the majority had more than 70% stenosis (80/95, 84%), and 9 chronic total occlusion of RCA).

Regarding the number of vessels involved we found that In 12 patients (52.2%) only one vessel was involved, in 10 patients (43.5%) two vessels were involved and in one patient only (4.3%) three vessels were involved, indicated that one vessel involvement was the more frequent, followed by two vessels and the least frequent was the three vessels involvement, P = 0.011. This is agreed with Villines et al [35] who found that the majority of patients with a CAC score of 0 and obstructive CAD had single-vessel disease (82%), with a lower prevalence of 2-vessel (12%) and 3-vessel (6%). Gulin et al [36] found that in patients with diabetes mellitus single-vessel CAD was observed in 26%, two-vessel in 41% and three-vessel in 32%, whereas in patients without DM, 52% single-vessel CAD, 30% two-vessel and 18 % three-vessel CAD

By comparing the severity of stenosis between the three arteries, no significant differences had been found in the three degrees of severity (mild, moderate and severe) between these arteries, in all comparison. In the reported literature no study is available for comparison with our results; further study is recommended for more evaluation of this finding.

In our study, we observed that the mean age of the patients with noncalcified atherosclerotic plaque (55.5years), was higher than the mean age of the cases without plaques (49.1years). Similarly, Ergün et al [30] and Kelly et al [33] found that the mean age of the cases with atherosclerotic plaque, as detected by coronary CT angiography were 53 and 54.4 years, respectively) and it was higher than the mean age of the cases without plaques (49 and 50.4 years, respectively). The results of our study demonstrated that the rate of plaque detection by coronary CT angiography in the patient population with a CAC score of zero was higher in patients over 40 years of age; however, it is difficult to determine a threshold value for the age limit because studies have reported that the risk for CAD is higher in patients 45–50 years of age [37].

In conclusion, CCTA can clearly demonstrate noncalcified atherosclerotic coronary plaques in a large group of patients with suspected CAD. The absence of coronary artery calcification does not exclude the presence of significant stenosis in symptomatic patients with no coronary Calcium.

Acknowledgment

We would like to thank the medical staff in the Department of Radiology in Al-Sader Medical City for offering the opportunities of this study. Thanks a lot to all patients who agreed to participate in this study.

Author Contribution

Dr. Kadhim did the study design, supervise data collection, writing part of the discussion and revising the manuscript; Dr. Al-Saadi participates in result interpretation, statistical analysis and writing part of the introduction and Dr. Hadi collect the data, writing the draft of the manuscript, interprets the results and made the statistical analysis.

Conflict of Interest

There is no conflict of interest for the authors of this manuscript and its potential publication.

Funding

No fund for this work.

References

1. Rumberger JA, Simons DB, Fitzpatrick LA, et al. Coronary artery calcium area by electron-beam computed tomography and coronary atherosclerotic plaque area: A histopathologic correlative study. Circulation. 1995; 92:2157-2162.
2. Sangiorgi G, Rumberger JA, Severson A, et al. Arterial calcification and not lumen stenosis is highly correlated with atherosclerotic plaque burden in humans: A histologic study of 723 coronary artery segments using nondecalcifying methodology. Am Coll Cardiol. 1998; 31:126-133.
3. Baumgart D, Schmermund A, George G, et al. Comparison of electron beam computed tomography with intracoronary ultrasound and coronary angiography for detection of coronary atherosclerosis. J Am Coll Cardiol. 1997; 30:57-64.
4. Russo V, Zavalloni A, BacchiReggiani ML, et al. Incremental prognostic value of coronary CT angiography in patients with suspected coronary artery disease. Circ Cardiovasc Imag. 2010; 3:351-359.
5. Budoff MJ, Achenbach S, Blumenthal RS, et al. Assessment of coronary artery disease by cardiac computed tomography: a scientific statement from the American Heart Association Committee on Cardiovascular Imaging and Intervention. Circulation. 2006; 114:1761-91.
6. O'Malley PG, Taylor AJ, Jackson JL, et al. Prognostic value of coronary electron-beam computed tomography for coronary heart disease events in asymptomatic populations. Am J Cardiol. 2000; 85:945-8.
7. Wong ND, Hsu JC, Detrano RC, et al. Coronary artery calcium evaluation by electron beam computed tomography and its relationship to new cardiovascular events. Am J Cardiol. 2000; 86:495-8.
8. Raggi P, Cooil B, Callister TQ. Use of electron beam tomography data to develop models for prediction of hard coronary events. Am Heart J. 2001; 141:375-82.
9. Kondos GT, Hoff JA, Sevrukov, et al. Electron beat tomography coronary artery calcium and cardiac events: a 37-month follow-up of 5635 initially asymptomatic low- to intermediate risk adults. Circulation. 2003; 107:2571-6.
10. Greenland P, LaBree L, Azen SP, et al. Coronary artery calcium score combined with Framingham score for risk prediction in asymptomatic individuals. JAMA. 2004; 291:201-5.
11. Arad Y, Goodman K, Roth M, et al. Coronary calcification, coronary disease risk factors, C-reactive protein, and atherosclerotic cardiovascular disease events: the St. Francis Heart Study. J Am Coll Cardiol. 2005; 46:158-65.
12. Taylor AJ, Bindeman J, Feueustein I, et al. Coronary calcium independently predicts incident premature coronary heart disease over measured cardiovascular risk factors: mean three-year outcomes in the Prospective Army Coronary Calcium (PACC) project. J Am Coll Cardiol. 2005; 46:807-14.
13. Budoff MJ, Shaw LJ, Liu ST, et al. Long-term prognosis associated with coronary calcification. J Am Coll Cardiol. 2007; 49:1860-70.
14. Detrano R, Guerci AD, Carr J, et al. Coronary calcium as a predictor of coronary events in four racial or ethnic groups. N Engl J Med. 2008; 358:1336-45.
15. Raggi P, Gongora MC, Gopal A, et al. Coronary artery calcium to predict all-cause mortality in elderly men and women. J Am Coll Cardiol. 2008; 52:17-23.
16. Greenland P, Bonow RO, Brundage BH, et al. ACCF/AHA 2007 clinical expert consensus document on coronary artery calcium scoring by computed tomography in global cardiovascular risk assessment and in evaluation of patients with chest pain: a report of the American College of Cardiology Foundation Clinical Expert Consensus Task Force (ACCF/AHA Writing Committee to Update the 2000 Expert Consensus Document on Electron Beam Computed Tomography) developed in collaboration with the Society of Atherosclerosis Imaging and Prevention and the Society of Cardiovascular Computed Tomography. J Am Coll Cardiol. 2007; 49:378-402.
17. Gill EJ. Does statin therapy affect the progression of atherosclerosis measured by a coronary calcium score? Curr Atheroscler Rep. 2010; 12:83-7.
18. Shareghi S, Ahmandi N, Young E, et al. Prognostic significance of zero coronary calcium scores on cardiac computed tomography. Cardiovasc Comput Tomograph. 2007; 1:155-9.

19. Greenland P, Bonow RO. How low-risk is a coronary calcium score of 0? The importance of conditional probability. Circulation. 2008; 117:1627-9.

20. Sarwar A, Shaw LJ, Shapiro MD, et al. Diagnostic and prognostic value of absence of coronary artery calcification. J Am Coll Cardiol. 2009; 2:675-88.

21. Cheng VY, Lepor NE, Madymoon H, et al. Presence and severity of noncalcified coronary plaque on 64-slice computed tomographic coronary angiography in patients with zero and low coronary artery calcium. Am J Cardiol. 2007; 99:1183-6.

22. Phillips LM, Mieres JH. Noninvasive assessment of coronary artery disease in women: what's next? Curr Cardiol Rep. 2010; 12:147-54.

23. Hausleiter J, Meyer T, Hadamitzky M, et al. Prevalence of noncalcified coronary plaques by 64-slice computed tomography in patients with an intermediate risk for significant coronary artery disease. J Am Coll Cardiol. 2006; 48:312-8.

24. Rubinshtein R, Gaspar T, Halon DA, et al. Prevalence and extent of obstructive coronary artery disease in patients with zero or low calcium score undergoing 64-slice cardiac multidetector computed tomography for evaluation of a chest pain syndrome. Am J Cardiol. 2007; 99:472-475.

25. Sosnowski M, Pysz P, Szymanski L, et al. Negative calcium score and the presence of obstructive coronary lesions in patients with intermediate CAD probability. Int J Cardiol. 2011; 148:16-18.

26. Buyukterzi M, Turkvatan A, Buyukterzi Z. Frequency and extent of coronary atherosclerotic plaques in patients with a coronary artery calcium score of zero: assessment with CT angiography. Diagn Interv Radiol. 2013; 19:111-118

27. Lloyd JD, Adams R, Carnethon M, et al. Heart disease and stroke statistics - 2009 update. A report from the American heart association statistics committee and stroke statistics subcommittee. Circulation. 2009; 119:480-486.

28. Budoff MJ. Prevalence of soft plaque detection with computed tomography. J Am Coll Cardiol. 2006; 48:319-21.

29. Choi EK, Choi SI, Rivera JJ, et al. Coronary computed tomography angiography as a screening tool for the detection of occult coronary artery disease in asymptomatic individuals. J Am Coll Cardiol. 2008; 52:357-365.

30. Ergün E, Koar P, Öztürk C, et al. Prevalence and extent of coronary artery disease determined by 64-slice CTA in patients with zero coronary calcium score. Int J Cardiovasc Imag. 2011; 27:451-458.

31. Kelly JL, Thickman D, Abramson SD, et al. Coronary CT angiography findings in patients without coronary calcification. Am J Roentgenol. 2008; 191:50-55.

32. Kitagawa T, Yamamoto H, Horiguchi J, et al. Characterization of noncalcified coronary plaques and identification of culprit lesions in patients with acute coronary syndrome by 64-slice computed tomography. JACC Cardiovasc Imag. 2009; 2:153-160.

33. Kiwasaki T., Matsumoto H. Aaono H., et al. Prevalence of noncalcified coronary plaque on 64-slice computed tomography in asymptomatic patients with zero and low coronary artery calcium. Can J Cardiol. 2010; 26(7):377-380.

34. Lu TM, Jou YL, Chen YH, et al. The clinical significance of right coronary artery stenosis on the prognosis of patients with unprotected left main disease undergoing percutaneous coronary intervention. Acta Cardiol Sin. 2011; 27:14-20.

35. Villines TC, Hulten EA, Shaw LJ, et al. Prevalence and severity of coronary artery disease and adverse events among symptomatic patients with coronary artery calcification scores of zero undergoing coronary computed tomography angiography. JACC. 2011; 58:2534-2540.

36. Gulin D, Galic E, Vrbanic L, et al. Distribution of coronary artery disease in acute coronary syndrome patients with diabetes mellitus. J Cardiothor Surg. 2013; 8(Suppl 1):P151.

37. Strong JP, Malcom GT, McMahan CA, et al. Prevalence and extent of atherosclerosis in adolescents and young adults: implications for prevention from the pathobiological determinants of atherosclerosis in youth study. JAMA. 1999; 281:727-735.

Correspondence to Dr. Mohammed A. Kadhim
E-mail: Dr_a_mohammed@yahoo.com
Received 25th Mar. 2015: Accepted 27th Sep. 2015