QUANTITATIVE CORONARY PLAQUE CHARACTERIZATION WITH MULTIDETECTOR CT ANGIOGRAPHY

Ahmed Mostafa Mohamed, Amir Louis Loka, Ali Hagag Ali, and Shaimaa Salah Mohamed*

Department of Radiology, Faculty of medicine, Ain shams University.

Corresponding :

Shaimaa Salah Mohamed Abdelrazik

Mobile: 1226009141

E mail:

Sheem1288@gmail.com

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ABSTRACT:

***Background**: Coronary artery disease (CAD) is a major cause of morbidity and mortality. Coronary atherosclerosis is a progressive disease with sudden destabilizing changes leading to plaque thrombosis and reorganization.*

***Aim of work:** Quantitatively characterize coronary atherosclerotic plaque composition in patients with CAD referred to Ain shams radiology department (El Demerdash Hospital) by using CT coronary angiography and compare prevalence of different plaque types.*

***Patients and Methods:** Seventy-eight patients of CAD symptoms (49 male, 29 female; mean age, 54.8 years) underwent CT coronary angiography (CTCA). Each patient underwent a non-contrast scan to determine the calcium score, then a contrast enhanced ECG gated scan. Coronary plaques were analysed as regard number, type, severity and plaque volumes by using semiautomated software.*

***Results:** 14 patients had normal CTCA, 37 patient had significant obstructive lesions, and 4 of them had a totally occluded coronary vessel. A total of 232 coronary vessel plaques were found. The number of patients with multi-vessel disease was significantly higher in diabetic patients verses non diabetics. Noncalcified plaques were more prevalent (than calcified plaques), in patients <55 years, where 56.4% of their plaques were noncalcified, however in patients >55 years only 39.3% of their plaques were noncalcified.*

***Conclusion:** Multi-slice CTCA is the non-invasive alternative to intravascular ultrasonography (IVUS) for plaque quantification, it is a reliable technique to detect CAD and estimate the degree of obstruction, number of affected vessels and the pattern of their affection. Using automated software provide the major advantage of higher reproducibility.*

***Keywords:** Coronary artery calcium (CAC), Coronary artery disease (CAD), Calcified coronary plaques (CCP), CT Coronary angiography (CTCA), Intravascular ultrasonography (IVUS), Left Circumflex coronary artery (LCX), Left anterior descending coronary artery (LAD), Left main (LM), Right coronary artery (RCA), Noncalcified plaques (NCP).*

INTRODUCTION:

Coronary artery disease remains a major cause of morbidity and mortality. Presence of atherosclerotic plaques in a coronary artery is responsible for lumen stenosis[1] .

Different imaging modalities are used to understand intracoronary plaques, such IVUS, IVUS with virtual histology (IVUS-

VH), elastography, intravascular Optical coherence tomography (OCT). Collectively, these technologies have the disadvantage of being inherently invasive[2].

There is a growing evidence to show that CTCA has good correlation with IVUS in the quantitative plaque analysis[3].

CTCA permits the non-invasive evaluation of the coronary atherosclerosis. CTCA provides information regarding the coronary tree, luminal narrowing, types of plaques, noncoronary cardiac and extracardiac thoracic abnormalities, including myocardial, pericardial, valvular and vascular lesions[4].

The assessment of coronary artery plaque composition and size are potentially more important than traditional detection of luminal stenosis in predicting devastating acute coronary events[5].

Non-calcified or low-attenuating plaques were more often seen in patients associated with acute coronary syndrome or development of major adverse cardiac events when compared to those with stable angina pectoris. Therefore, assessment of non-calcified plaque in terms of total plaque volume has significant clinical value[3].

Coronary calcification alone can underestimate total plaque burden. Noncalcified plaques, play a crucial role in the development of acute coronary syndrome (ACS) and sudden thrombotic occlusion[6].

Prior Percutaneous coronary interventions, CTCA can be helpful in detecting low attenuating plaques (lipid rich ones) which may cause periprocedural distal emboli (following balloon dilatation), thus may help in shifting Percutaneous coronary intervention strategy toward the use of direct stenting, stronger antithrombotic therapy or preprocedural statin therapy for plaque stabilization[7].

CTCA provides information regarding the coronary tree in order to develop personalized medical care to enable therapeutic interventions[5].

By the help of semiautomated plaque analysis software, we can obtain accurate and reproducible quantitative measurements, in order to facilitate the serial assessment of atherosclerotic burden by CTCA[8] .

AIM OF WORK:

Quantitatively characterize coronary atherosclerotic plaque composition in patients with CAD referred to Ain shams radiology department (El Demerdash Hospital) by using CT coronary angiography and compare prevalence of different plaque types.

PATIENTS AND METHODS:

A total number of 78 patients with symptoms of coronary artery disease were scheduled for elective CTCA between September 2017 and January 2019. Patients were referred to CTCA to investigate recent onset of dyspnea on exertion, fatigue on mild effort or ischemic chest pain (retro-sternal heaviness or squeezing sensation that may radiate to the left arm, neck, back or lower jaw).

The exclusion Criteria:

- patients with known severe contrast allergy
- renal dysfunction with serum creatinine > 2 mg/dL
- previous bypass operation
- unstable clinical condition (severe heart failure, severe pulmonary disease)
- contraindications to β-blockers (bronchial asthma)
- inability to perform a 10-second breath hold
- patients with uncontrolled arrhythmia
- pregnant females

All patients were subjected to the following:

- Obtaining an informed consent
- Full history: Including history of systemic hypertension, DM and smoking
- Reassurance of the patient was done and all steps of the study were explained in detail to each patient.
- Intravenous access was established in a cubital vein.
- One-hour pre-examination, patients received oral beta-blocker to reduce the heart rate. Sublingual nitroglycerin was administered prior to the scan (0.4-0.8 mg dose)

Scanning parameters and image acquisition:

Patients underwent CTCA using MDCT scanners (80 slice, Aquilion Lighting, Toshiba medical systems and 128 slice, OPTIMA, GE health care), at Ain Shams university hospitals (El Demerdash hospital), Radiology department.

(1) A noncontrast scan was performed to determine the calcium score

(2) The contrast-enhanced scan was obtained within one single breath-hold, using either a retrospective electro-cardiogram (ECG)-gated protocol or prospectively with ECG-triggering depending on patient's heart rate. A bolus of 370 mg/mL iodinated contrast material was injected intravenously followed by a 30 mL saline flush. Reconstructions were performed at 40%, 75%, and 80% phases of the R-R interval period.

Image analysis:

CT data were transferred to workstations (AW volumeshare 7, GE medical systems and 3D synapse, Fujifilm).

Total calcium scores for the patients were calculated and expressed by Agatston score. The Agatston score calculates the total amount of calcium on the basis of the number, areas and peak Hounsfield units (HU) of the detected calcified lesions.

Coronary trees were analysed using 17 segment model. Only the major epicardial vessels were considered for analysis. Manual tracing of the coronary segments is done to detect plaques, followed by semi-automated quantification of different types of plaques.

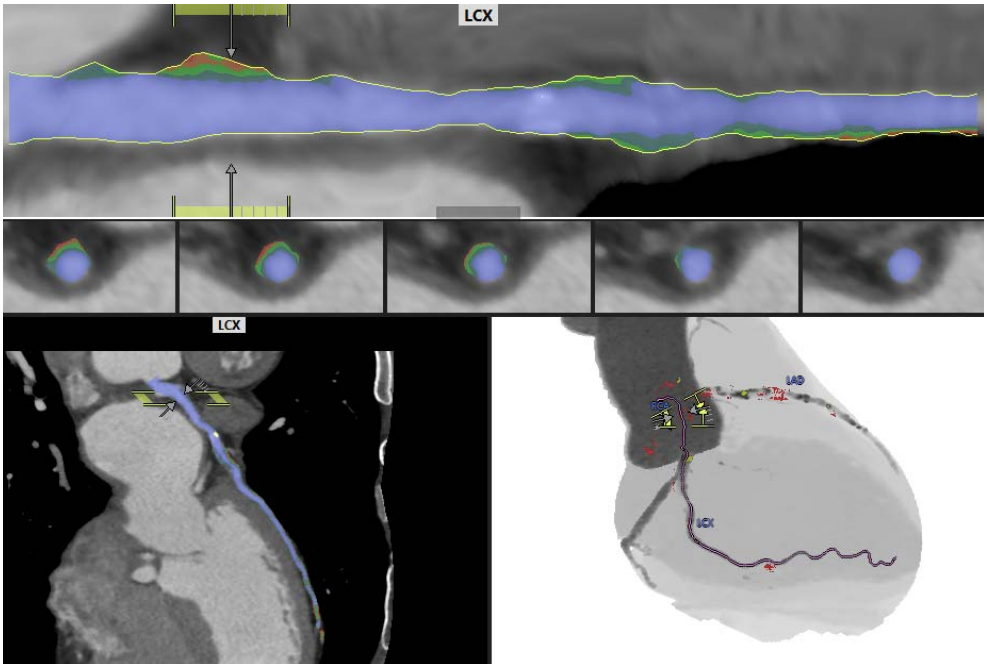
Plaques were classified into; (i) non-calcified plaque: with no detectable calcium; (ii) mixed plaque: calcified tissue occupying 50% of a single cross-section within it; (iii) calcified plaque: calcified tissue occupying ≥ 50% of a single cross-section within it.

Software CT image colour coding was helpful, depending on Hounsfield units (HU), to better differentiate the plaque characteristics. Hounsfield units -50 to-1 coded red , indicating fatty tissue , HU 0 to 29 were coded orange , indicating a super soft spot; HU 30 to 129 were coded green and dark green , indicating a soft plaque; Hounsfield units 500 to 800 were coded yellow, indicating calcification; and HU 130 to 499 were coded as blue , indicating a contrast-filled lumen (Diagram. 1).

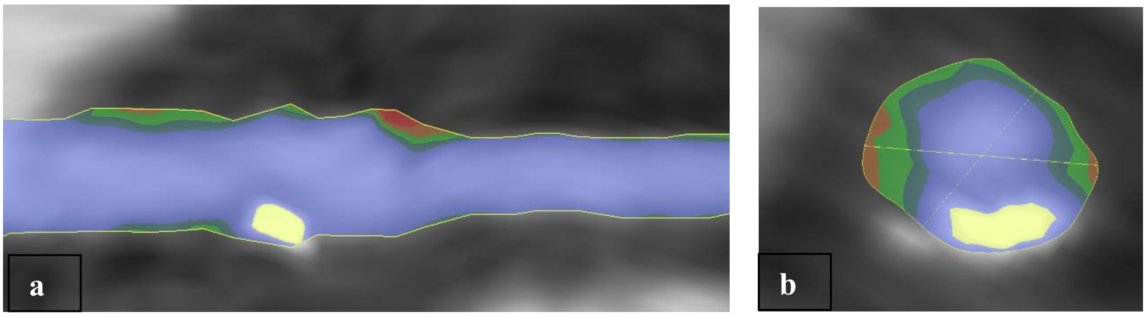
The colour coding described above was able to produce the plaque images; calcified plaque (coded yellow), non-calcified plaque (coded green and dark green)

Volume of different types of plaques was automatically calculated, by subtracting the lumen volume from the outer wall volume, and expressed in mm^3(Diagram. 2).

Atherosclerotic lesions were quantified for stenosis by visual estimation. The severity of luminal-diameter stenosis was divided into nonobstructive plaques (≤50%luminal stenosis) and obstructive plaques (>50% luminal stenosis).



Diag. (1): Segmentation of LCX a with vascular model and coronary cross sections. Plaque volume is the sum of all plaque component volumes.



Diag. (2): Automated plaque detection. Vessel MPR(a), cross section (b), with calcified (posterior wall) and soft plaques (anterior, lateral wall).

RESULTS

Population Demographics

The study population consisted of 78 patient, presented with symptoms of coronary artery disease. The sample was 37.2% female, 62.8% male. 51.3% of patients were hypertensive, 46.2% were diabetic and 39.7% were smokers. Population demographics and CAD risk factors by the presence or absence are shown in Table 1.

Table (1): Population demographics and CAD risk factors by the presence or absence

		No. = 78
Age	Mean ± SD	54.86 ± 7.82
	Range	37 – 75
Gender	Female	29 (37.2%)
	Male	49 (62.8%)
Smoking		31 (39.7%)
HTN		40 (51.3%)
DM		36 (46.2%)

Prevalence of Coronary Plaque

Among 78 patients, 14 (17.9%) had normal CTCA, 21(26.9%) had three vessel disease and 2(2.6%) had three vessel with LM affection. 37 patient had significant obstructive lesions, and 4 of them had a totally occluded coronary vessel.

The prevalence of coronary plaque increased with age Table 2. The prevalence of coronary plaque was significantly higher after age 55 years. The prevalence of coronary plaque increased in men, where multivessel affection was significantly higher (Table 3).

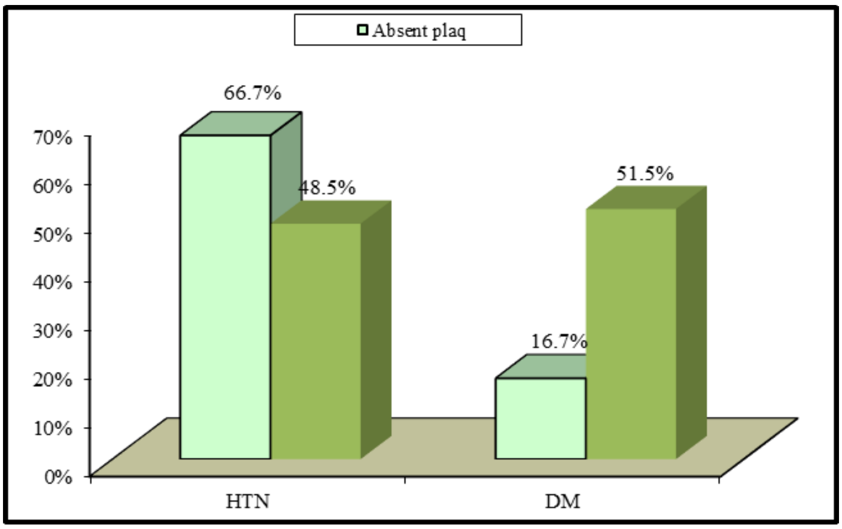
Table (2): The prevalence of coronary plaque by age.

		Age <55	Age ≥55	Test value	P-value	Sig.
		No. =35	No. = 43			
plaque	Absent	10 (28.6%)	2 (4.7%)	8.481	0.004	HS
	Present	25 (71.4%)	41 (95.3%)			
No. of vessels affected	0	10 (28.6%)	4 (9.3%)	9.740	0.045	S
	1	10 (28.6%)	7 (16.3%)			
	2	9 (25.7%)	15 (34.9%)			
	3	6 (17.1%)	15 (34.9%)			
	4	0 (0.0%)	2 (4.7%)			

Table (3): Gender and coronary vessel plaques.

		Female	**Male**	**Test value**	**P-value**	**Sig.**
		No. = 29	**No. = 49**			
No. of vessels affected	0	8 (27.6%)	6 (12.2%)	10.598*	0.031	S
	1	10 (34.5%)	7 (14.3%)			
	2	7 (24.1%)	17 (34.7%)			
	3	4 (13.8%)	17 (34.7%)			
	4	0 (0.0%)	2 (4.1%)			

Among patients with positive coronary plaques, 34 (51.5%) were diabetic, while 32 (48.5%) were not diabetic, P-value <0.05: Significant. And 32 (48.5%) were hypertensive (Diagram 3). Diabetic patients show a statistically significant higher incidence of multivessel affection than nondiabetic patients (75% vs. 45%, P value < 0.05).



Diag. (3): Bar chart representation of patients with positive risk factors.

Coronary artery calcium (CAC)

The distribution of patients according to different Agatston scores is shown in Table 4. Among 16 patients who had zero CAC Score, 6 patients (37.5%) had CAD (with 15 non-calcified plaques, and mean plaque volume burden =220), while 10 (62.5%) had normal CTCA.

Patients >55 years old had a strong statistical significance of higher CAC than those <55 years (Median 58 in Patients >55 year Vs 4 in Patients >55 year, P-value <0.05).

Table (4): distribution of patients according to different Agatston scores

AG Score	No. = 78
0	16 (21%)
1-10	18(23%)
11-100	25(32%)
101-400	16(82%)
>400	3(3.80%)

Type of plaques

We found 232 lesions, among them, calcified plaques were the most common which represent 49.1%, then non-calcified plaques were 41.3%, while mixed plaques represented only 9.4%. (Table 5,6&7)

Table (5): Calcified plaques and their distribution among coronary vessels

Calcified	No. = 114	
LAD	٤٨(42.1%)	
LM	7 (6.1%)	
LCX	٣8 (33.3%)	
RCA	٢١(18.4%)	
Total plaque Volume 1724 mm^3	Median (IQR)	17.85 (8 - 57)
	Range Mean	4 – 111 15

Table (6): Non-Calcified plaques and their distribution among vessels

Non-Calcified	No. = 96	
LAD	٤6(47.9%)	
LM	4 (4.1%)	
LCX	12 (12.5%)	
RCA	34(35.4%)	
Total plaque Volume 12670	Median (IQR)	180 (80 - 326)
	Range Mean	13 – 860 132

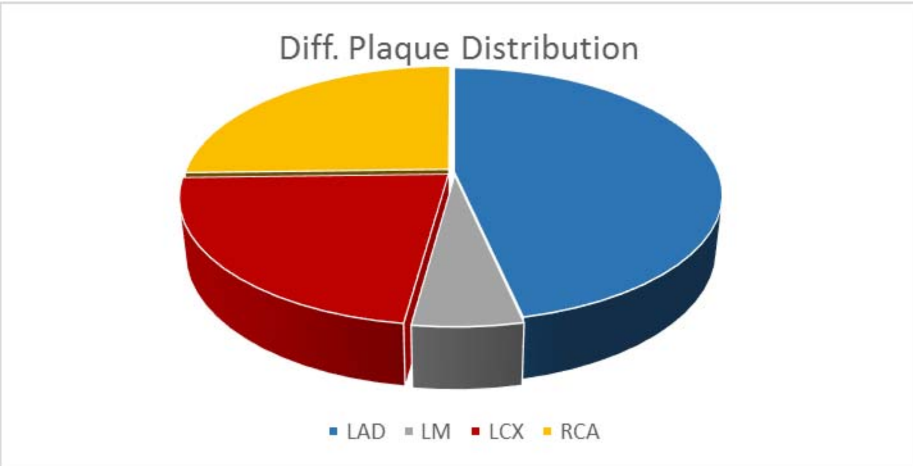
Table (7): Mixed plaques and their distribution among vessels

Mixed	No. = 22	
LAD	1٤(63.6%)	
LM	2 (9%)	
LCX	2 (9%)	
RCA	4(18%)	
Total plaque Volume 3108	Median (IQR)	147 (34.5 - 255)
	Range Mean	17– 664 141

Table (8): Plaque burden volumes of NCP and CCP by gender

		Female No. = 29	Male No. = 49	Test value	P-value	Sig.
Calcified						
Volume mm^3	Median (IQR)	23 (8 – 57)	16 (8 – 57)	-0.293‡	0.769	NS
	Range	7 – 66	4 – 111			
Non calcified						
Volume mm^3	Median (IQR)	80 (28 – 133)	310 (165 – 560)	-3.939‡	0.000	HS
	Range	13 – 154	21 – 860			

A total of 312 coronary vessel, harboring 232 plaque. The most commonly affected vessel was the LAD artery 46.5% , vs. 25.4% RCA , 22.4% LCX and 5.6% LM (Diagram 4).



Diag. (4): Pie chart of percentage of coronary vessel affection

The plaque burden volumes of NCP and CCP by age and gender (Tables 8&9). NCP volume was strongly associated with male gender.

Table (9): Plaque burden volumes of NCP and CCP by age

		Age <55 Patient No. = 35	Age >55 Patient No. = 43	Test value	P-value	Sig.
Calcified						
Volume mm^3	Median (IQR)	19.7 (8 - 92)	16 (8 - 46)	-0.820	0.412	NS
	Range	5 – 95	4 – 111			
Non calcified						
Volume mm^3	Median (IQR)	184.5 (90 -560)	180 (67- 326)	-0.516	0.606	NS
	Range	21 – 1000	13 – 860			

Importantly, noncalcified plaques were more prevalent than calcified plaques, in those <55 years old, in whom 56.4% of their plaques were noncalcified, however, in patients >55 years old only 39.3% of their plaques were noncalcified.

DISCUSSION

In the present study we found that the frequency of CAD among patients complaining from recent chest pain was 82.05%. Among 78 patients we found 17.9% having normal CCTA, 47.4% having significant CAD. In study conducted by Koulaouzidis et al.,2012 "CTCA as Initial Work-Up for Unstable Angina Pectoris" they found that among 43 patients 17 (39.5%) had normal CTCA, and only 4 (9.3%) had a significant obstructive lesion[9].

In our study, Patients with two vessel disease were 30.8%, 26.9% had three vessel disease and 2.6% had three vessel and diseased LM.

Zero calcium score was detected in 16 case, however 37.5% of them show CAD. In 2011, Villines et al., noted in their study, that 16% of patients with zero CAC scores had CAD (13% had nonobstructive stenosis, 3% had >50% stenosis). Patients with CAC scores of 0 have not yet developed detectable calcified coronary lesion, but they can have fatty streaking and early stages of plaque, non-calcified plaques up to obstructive disease. Noncalcified plaques are common in many young adults [10].

In this present study, we found that patients > 55 years old had a statistically significant higher CAC score than those < 55 years old (Median 58 Vs 4, P-value <0.05), while no statistically significant difference in CAC score between males and females.

We found that males show a statistically significant higher incidence of multivessel affection than females (73% vs. 38%, P value < 0.05). In 2010, Chu et al. ,stated that CT findings of CAD between men and women were nearly similar except that men had more calcified plaques (p < 0.05)[11].

In our study, we found that diabetic patients show a statistically significant higher incidence of multivessel affection than nondiabetic patients (75% vs. 45%, P value < 0.05). In 2010, Van Werkhoven et al., stated that diabetic patients showed a higher average number of diseased coronary segments (5.6 vs. 4.4, P = .001), weather obstructive or non-obstructive CAD [12].

In our 78 patients, we found 232 coronary lesions, there were 9.5% mixed plaques, 49.1% calcific plaques, and 41.3% with soft plaques. The most common diseased coronary vessel was the LAD artery 46.5%, vs. 25.4% RCA, 22.4% LCX and 5.6% LM. in 2015, Diaz-Zamudio et al, examined 56 coronary artery lesions, 64.3% were in the LAD, 26.8% were in the right coronary artery, and 8.9% were in the left circumflex coronary artery[13].

Noncalcified plaques were more prevalent than calcified plaque in those <55 years old, in whom 56.4% of the plaques were noncalcified. In 2014, Kral et al., stated that in patients <55 years old, 75% of the plaques were noncalcified. It is noteworthy that coronary calcium may markedly underestimate the total plaque burden in this population[14].

Moreover, CAC score is not a useful marker for assessing the reduction of plaque after therapy, likely because CAC does not accurately reflect a change in modifiable noncalcified plaque.

The plaque burden volumes of NCP were significantly higher in males (median 310mm^3 Vs 80mm^3 n females), with no significant difference in plaque volumes in different age groups.

The mean of plaque volumes in our study was 132mm^3 non-calcified plaques, and 15mm^3 calcified plaques. In 2011, Rinehart et al., calculated mean of plaque volumes was 223 mm^3 non-calcified plaques, and 39 mm^3 calcified plaques. [15].

The ability of CTCA to assess and characterize atherosclerotic plaque can help interventional cardiologist in planning percutaneous coronary intervention strategies.

Using automated plaque quantification methods is supposed to reduce interobserver variability when compared to manual quantification techniques.

Limitations of this study include a relatively homogeneous population, as collected from a single site, with limited variation. Patients with severe renal failure were not eligible for coronary CT angiography. Measurement of plaque volume can be affected by technical factors such as tube voltage and contrast material injection rate.

Conclusion

Multi-slice CT coronary angiography is the non-invasive alternative to IVUS for plaque quantification, it is a reliable technique to detect CAD and estimate the degree of obstruction, number of affected vessels and the pattern of their affection. Using automated software provide the major advantage of highly reproducible assessments of lumen area, minimal lumen diameter, plaque burden, plaque volume and can be used in following the response to therapy.

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التوصيف الكمي للترسبات داخل الشرايين التاجية باستخدام الاشعة المقطعية متعددة المقاطع

أحمد مصطفي محمد، أمير لويس لوقا ، علي حجاج علي ،.شيماء صلاح محمد عبدالرازق.

(قسم الأشعة التشخيصية مستشفيات جامعة عين شمس)

المقدمة: مرض الشريان التاجي هو سبب رئيسي للامراض والوفيات. تصلب الشرايين التاجي هو مرض يمكن ان يتطور و مع التغيرات المفاجئة يمكن ان يحدث تجلط فوق التصلبات داخل الشريان .

الهدف من الدراسة : تميز تكوين الترسبات داخل الشرايين التاجية في المرضى الذين يعانون من أعراض مرض الشريان التاجي بقسم الأشعة مستشفي الدمرداش (عين شمس) و مقارنة انتشار الأنواع المختلفة بواسطة الأشعة المقطعية.

المرضى وطرق البحث: ثمانية وسبعون مريض (الرجال ٤٩ ، النساء ٢٩ ومتوسط العمر ٥٤,٨سنوات) خضعوا للفحص بالاشعة المقطعية علي الشرايين التاجية .كل مريض خضع لفحص بدون صبغة لتحديد كمية الكالسيوم، يتبعه فحص بالصبغة ثم تحليل لاي لوحة تصلب من حيث العدد والنوع ونسبة ضيق الشريان و كمية الترسبات في الشرايين التاجية باستخدام برامج التحليل.

النتائج: ١٤ مريضا كان الفحص سلبي و٣٧ مريض عندهم ترسبات كثيفة (تضيق الشرايين)و ٤ منهم لديهم شرايين مغلقة تماما .تم العثور على إجمالي ٢٣٢ ترسب في الشرايين التاجية. عدد المرضى اصحاب الشرايين المصابة كان أعلى بكثير في مرضى السكري .اللويحات غير المتكلسة كانت اعلي انتشارا بين الفئة العمرية الصغيرة(< ٥٥سنة).

الخاتمة: الاشعة المقطعية متعددة المقاطع لتصوير الشرايين التاجية هي بديل القسطرة الغازية للتمييز الكمي لترسبات الشرايين و هي تقنية موثوقه لتقدير درجه الانسداد ، وعدد الشرايين المتضررة و تكوين الترسبات .استخدام برمجيات التحليل توفر الميزة الرئيسية لتقليل الخطأ في اعادة القراءة .