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Quantification of Non-Calcified and Calcified Coronary Plaques Using 64-Slice MDCT in Patients with Acute Coronary Syndrome

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Abstract:

Purpose: To investigate the accuracy of 64-row MDCT to analyze and quantify coronary arterial plaques in patients presented with acute coronary syndrome (ACS).

Patients and methods: Between April 2010 and December 2013, 50 patients presented with acute cardiac chest pain were categorized into 2 groups according to their diagnosis based on clinical evaluation, ECG findings and cardiac biomarkers; group A including patients with ACS and group B including patients with stable angina (SA). Both groups underwent 64-row multidetector CT (MDCT) coronary arterial imaging. For each plaque, stenosis percentage was evaluated and the plaque was quantified using software (Sureplaque®) based on the density (HU) and percentage of its individual components including lipid, soft tissue, and calcium density.

Results: Of the 50 patients; 24 and 26 were grouped into groups A & B respectively. The mean value of stenosis percent of the proximal & middle coronary segments of group A patients = 77.2% ± 10.2% - 90.5% ± 58.4% and 79.5% ± 9.1% - 85.25% ± 11% respectively, while in group B = 54.1% ± 12.1% - 65.2% ± 18.4% & 53.3% ± 1.5% - 68.6% ± 11.7% respectively (p=0.00-0.001). Quantification showed a mean value of lipid content percentage of group A = 15.4% ± 0.8% - 47.7 % ± 19.2 %, while in group B = 7.2% ± 5.5% - 10.3% ± 8.2% (p=0.008–0.001). The mean value of soft tissue content percentage in group A = 15.4% ± 0.8% - 47.7 % ± 19.2 %, while in group B = 7.2% ±5.5% - 10.3% ± 8.2%. The calcification content percentage in group A = 18% ± 8.7% - 35.1 % ± 16 %, while in group B = 66.4% ± 13.8% - 76.7% ± 16.5%.

Conclusion: 64-row MDCT angiographic quantification software provides a good basis for the future attempts of proper risk stratification of patients with coronary artery disease especially those liable for developing ACS.

Keywords: Acute coronary syndrome, Stable angina, coronary plaques, coronary MDCT angiography, plaque quantification.

Introduction:

Acute coronary syndromes (ACS), especially myocardial infarction and sudden cardiac death, are mostly caused by rupture or erosion of coronary atherosclerotic plaques. The plaque itself does not have to be associated with lumen narrowing. Coronary blood flow may be obstructed by a thrombus forming at the site of plaque rupture. In fact, the majority of lesions that cause acute coronary syndromes are not stenotic before the event occurs [(1)].

Hence, in acute coronary syndromes, the culprit lesion is often a plaque complicated by thrombosis extending into the lumen. Such plaques are termed "thrombosed plaques". In some cases, multiple thrombosed plaques may exist, only one of which is acting as the "culprit" lesion. A plaque may also develop thrombosis, which remains asymptomatic due to the presence of collaterals, or failure of the thrombus to significantly impede blood flow [(2)].

Disrupted plaques provoke thrombosis in several ways. First, contact with collagen in the plaque's extracellular matrix can trigger platelet activation. Second, tissue factor (TF) produced by macrophages and smooth muscle cells (SMCs) activates the coagulation cascade [(3)].

A noninvasive technology gaining clinical acceptance is computed tomography angiography (CTA). It is used primarily for the detection of calcium; however, it has been shown that it is also useful in detecting the plaques that may be responsible for ACS. Therefore, patients with coronary lesions exhibiting positive remodeling and low attenuation on CT angiography were considered at higher risk for ACS compared with patients having lesions without these characteristics[(4)].

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As a result, direct noninvasive quantification of coronary atherosclerotic plaque morphology and burden may be important for improving cardiovascular risk stratification and for monitoring the course of coronary artery disease [(5)].

One of the most serious problems with cardiac CT scanning is due to inevitable motion artifacts owing to the continuous cardiac motion. Hence, gating techniques are used to improve temporal resolution and minimize motion artifacts. Two approaches to cardiac gating are typically used: prospective ECG triggering and retrospective ECG gating [(6)].

Using 64-slice MDCT scanners allow for the additional advantage of rapid scanning of the cardiac anatomy, requiring minimal patient cooperation (short breath hold), and improved image quality (better spatial and temporal resolution) with higher diagnostic accuracy [(7)].

Several multi-center trials supported the high sensitivity of coronary CT angiography; however, specificity might be reduced, particularly among patients with severe coronary artery calcification (which can render CT angiography un-interpretable, particularly at calcium scores above 400 to 1000) or obesity (due to excess image noise)[(8)].

Several studies have discussed the potential of using MDCT angiography for detection and analysis of coronary plaque composition. However, in vivo studies have consistently concluded that CT values vary widely for non-calcified plaque components. Although mean values were often significantly different between fibrous and lipid rich plaques, a substantial overlap of Hounsfield units was reported, precluding reliable characterization of individual non-calcified plaques [(9)].

Software algorithms that can volumetrically quantify calcified and non-calcified atherosclerotic plaque components were introduced to permit the use of multidetector CT in risk stratification and monitoring therapies designed to manage and reduce risk of major adverse cardiac events [(17)]. More recently, automated segmentation tools for plaque quantification have been introduced by all manufacturers, with a reported improved inter-observer variability between 12%–17% [(10)].

Patients and methods:

Our study was carried out between April 2010 and December 2013 on 50 patients presented to the emergency room of Ain shams university and Ain shams university specialized hospitals, with acute chest pain of cardiac origin and an initial diagnosis of ACS. All patients underwent clinical examination, ECG, and cardiac enzyme (CK-MB &/or troponin-I) assessment.

Based on the clinical examination, ECG and cardiac enzymes, the patients were grouped according to their final diagnosis into 2 groups; group A with ACS and group B with SA. Inclusion criteria for group A included: diagnostic ECG changes for myocardial infarction (ST-segment elevation or depression 1 mm or T-wave inversion 4 mm in 2 anatomically contiguous leads), and elevated troponin-I and/or creatine kinase-MB levels. Inclusion criteria for group B included: 5 min of persistent chest pain within the previous 24 h, with no or non-diagnostic ECG changes and normal initial cardiac biomarkers, with improvement of nitroglycerin administration.

All patients were hospitalized, properly managed and the cardiac symptoms were stabilized prior to performing cardiac CT imaging. The patients with severe arrhythmias refractory to medical treatment, heart rate above 75 after β-blocker administration, heavily calcified lesions by visual estimates, contraindication to iodinated contrast media administration, were excluded from the study. Before the cardiac imaging was performed heart rate control was done by administering 50 - 100 mg of atenolol (Tenormin®) orally, half to one hour before the procedure for patients with heart rate above 60 bpm, while patients with heart rate <60 bpm no β-blockade was done. Patients who experienced remarkable anxiety received an oral benzodiazepine; 1.5 mg bromazepam 15 – 30 minutes before the scan. An IV access was also secured (using an 18 G cannula).

The scans were performed using a Toshiba multislice Aquilion 64 system (Toshiba Medical Systems, Otawara, Japan). First a non-contrast calcium scoring study was performed using prospective ECG triggering, with beam collimation of 4 × 3.0 mm, rotation time 500 ms., tube current and voltage of 200 mA and 120 kV. The contrast enhanced coronary angiography was commenced directly afterwards via injecting 50

ml of contrast through the IV line using a dual head injector, followed by a 50 ml of saline chaser. The injection rate was set at 5 ml/sec for both the contrast and the saline. The scan was performed using an X-ray beam collimation width of 32 mm (0.5-mm slice thickness × 64 rows) with the spatial resolution in x-, y-, and z-axes of 0.35 mm, a gantry rotation of 350 milliseconds, a pitch of 11.2–13.2, an electric current of 350–450 mAs, and a tube voltage of 120–135 kV (depending on patient size).

The raw data were transferred to a workstation (Vitrea ® - Vital, Opus Parkway, Minnetonka, Minnesota) where the datasets were reconstructed at a slice thickness of 0.5 mm with 0.3 mm increments using ECG gated reconstruction in the diastolic phase (75% of the R-R interval). The whole coronary tree was reviewed for motion artifacts, if there were any, other phases of reconstruction were done including systolic phase. The datasets were then displayed and analyzed using several modes of presentation; axial images, MPR (Multi-Planar Reformat), oblique MPR, curved MPR, MIP (maximum intensity projection) as well as VRT (Volume Rendering Technique) formats. Plaque quantification was done using a semi-automated density plaque-tracing tool using the difference of attenuation values of the different plaque components as well as the lumen density, set by predetermined threshold values (Sureplaque ®). The resulting images were demonstrated as a color overlay of the curved MPR images of the questioned vessel/vascular segment, as well as calculation of the stenosis percentage by using area method, plaque volume, and volume percentages of the different components of the marked plaque based on preset HU thresholds.

Based on the anatomical coronary segment model, the coronaries were anatomically divided into 17 segments where the patients with ACS were examined for only culprit lesions, found in concordance with the ECG findings of the patients (i.e. wall involvement) while patients presented with stable angina were examined for all coronary plaques found causing > 40% vascular stenosis.

Statistical analysis was done using Statistical package for Social Science (SPSS v22.1 for windows; SPSS Inc., Chicago, IL) software, using mean, standard deviation (± SD) and range for parametric numerical data, while median was used for non –parametric numerical data. Frequency and percentage (%) were used for non-numerical data. Independent sample Mann-Whitney U-test was used to assess the statistical significance of the difference between two study group means using non-parametric variables. Non-parametric independent samples Kruskal-Wallis test was used for analysis of variance between categories with non-parametric values & Spearman's test for bivariate correlation of non-parametric values.

Results:

50 patients were enrolled in our study, with their demographic criteria summarized in table 1.

Demographic data		Number of patients
Sex	Males	25
	Females	25
Risk factor	Dyslipidemia	30
	Diabetes Mellitus	29
	Hypertension	29
	Smoking	24
Mean age	Males	58.1 ± 11.6
	Females	57.5 ± 11.8
Diagnosis	ACS	24
	SA	26

Table (1): Summary of the demographic criteria of the study group.

The CT scanning resulted in visualization of 650 coronary arterial vascular segments, with 143 segments containing atherosclerotic plaques, distribution of the plaques according to the vascular segments are described in table 2

Artery segment	Number of segments with visualized plaques	Number of segments not visualized or with no visualized plaques	Total
pRCA	21	29	650
mPCA	15	35	
dRCA	0	50	
LM	8	42	
pLAD	24	26	
mLAD	20	30	
dLAD	0	50	
pLCx	18	32	
mLCx	12	38	
dLCx	2	48	
OM 1	9	41	
OM2	3	47	
D 1	11	39	
Total	134	507	

Table (2): Plaque distribution among the coronary arterial segments

For each group the coronary arterial tree was assessed for the total calcium (calcium scoring), and the individual plaques were assessed for luminal stenosis percentage, and plaque composition.

Calcium scoring: The Calcium score for cases presented with ACS had a mean value of 167.6 ± 61.3 and cases presented with SA had a mean value of 250.2 ± 95.8, yet no statistically significant differences were found between the 2 groups (p=0.481).

Luminal stenosis: The images had excellent quality for estimation of the luminal stenosis percent for the proximal and middle coronary segments whereas it had poor diagnostic quality for the distal segments. The p-values for 5 out of 7 proximal and middle vascular segments were highly significant (p=0.00-0.01) between both groups. The values for luminal stenosis percentage and p-values are listed in tables 3 and 4.

	Acute coronary syndrome				Stable Angina				P-value
	No.	Mean	±	SD	No.	Mean	±	SD	
pRCA	5	77.2	±	10.2	16	65.2	±	12.8	0.064
Left main	0	NA			8	54.1	±	12.1	NA
pLAD	2	90.5	±	2.1	22	58.4	±	16.8	0.001*
pLCx	2	89	±	0	16	55.6	±	15.3	0.00*

Table 3: The mean values for stenosis percentages of the proximal coronary arterial segments (*=significant).

Arterial segment	Acute coronary syndrom				Stable Angina				P-value
	No.	Mean	±	SD	No.	Mean	±	SD	
m-RCA	5	83.8	±	7.4	10	64.7	±	12.6	0.003*
m-LAD	4	79.5	±	9.1	16	68.6	±	1.4	0.09
m-LCx	4	85.2	±	11	8	60.7	±	11.4	0.01*
OM 1	0	NA			9	54.2	±	12.5	NA
OM 2	0	NA			3	53.3	±	1.5	NA
D 1	0	NA\			11	61.8	±	18.3	NA

Table 4: The mean values for stenosis percentages of the middle coronary arterial segments (*=significant).

Plaque analysis: CT images were of overall excellent diagnostic quality for the proximal coronary segments, and of good quality for the middle vascular segments, however CT images of the distal vascular segments were of poor diagnostic quality except for two cases where the distal LCx, and distal LAD were successfully quantified.

The mean value of lipid content percentage in cases with ACS ranged from 15.4% ± 0.8% to 47.7 % ± 19.2 %, while in cases of stable angina, the percentage ranged from 7.2% ± 5.5% to 10.3% ± 8.2%. 5 out of 6 proximal and middle coronary segments showed highly significant p-values for the lipid content percentage (p=0.00-0.013), between both study groups. The results are shown in table 5.

	Acute coronary syndrome				Stable Angina				Mann-Whitney U test
	N	Mean	±	SD	N	Mean	±	SD	p-value
p-RCA	5	35.2	±	16.0	16	8.5	±	5.3	0.00*
LM	0	NA			8	8.4	±	6.3	NA
p-LAD	2	15.4	±	0.8	22	7.2	±	5.5	0.065
p-LCx	2	40.2	±	12.9	16	8.5	±	6.6	0.013*
m-RCA	5	42.6	±	7.6	10	9.3	±	6.5	0.001*
m-LAD	4	38.8	±	5.5	16	9.1	±	4.1	0.00*
m-LCx	4	47.7	±	19.2	8	10.3	±	8.2	0.008*

Table (5): Distribution of the mean percentage values of lipid plaque contents of the proximal and middle coronary segments in cases of ACS and SA. (*=significant)

The mean value of soft tissue content percentage in cases presented with ACS ranged from 15.4% ± 0.8% to 47.7 % ± 19.2 %, while in cases of stable angina, the percentage ranged from 7.2% ±5.5% to 10.3% ± 8.2%. Only 2 out of vascular 7 segments showed significant differences between the 2 study groups for their soft tissue composition. Results listed in table 6

	Acute coronary syndrome				Stable Angina				Mann-Whitney U test
	N	Mean	±	SD	N	Mean	±	SD	p-value
p-RCA	5	46.8	±	18.7	16	20.4	±	7.7	0.006*
LM	0	NA			8	17.7	±	6.4	NA
p-LAD	2	50	±	1.7	22	21.3	±	6.4	0.007*
p-LCx	2	25.1	±	6.8	16	25.1	±	8.8	0.83
m-RCA	5	26.6		11.2	10	20.2		5.7	0.31
m-LAD	4	26.1		16.3	16	22.4		8.9	0.82
m-LCx	4	29.8		16.4	8	21.7		10.7	0.46
OM 1	0	NA			8	20.6		8.8	0.46

Table (6): Distribution of the mean percentage values of soft tissue plaque contents of the proximal & middle coronary segments in cases of ACS and SA.

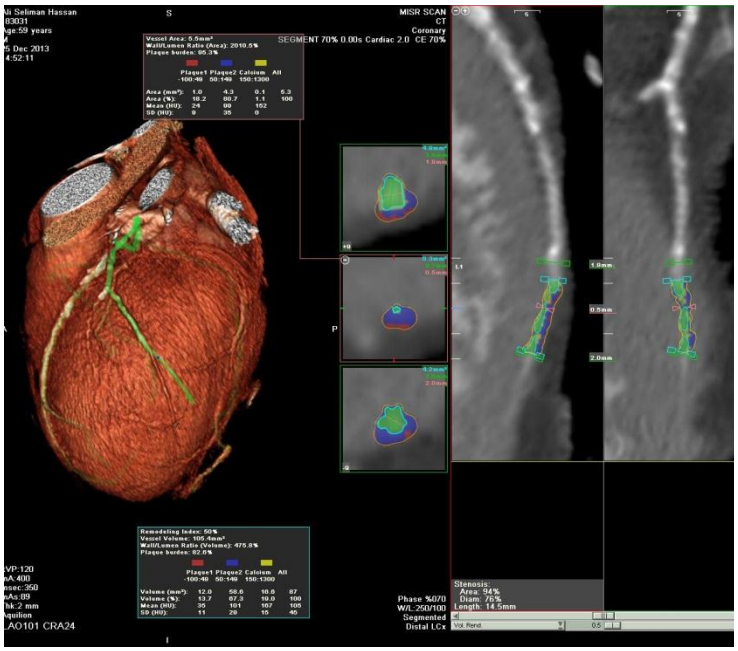
As regards the pattern of plaque calcification; the diffuse calcification pattern had a prevalence of 8.3% for cases with ACS, and 80.7% for cases with SA. On the other hand the Spotty calcification pattern had a prevalence of 91.6% for cases with ACS and 19.2% for cases with SA. There were statistically significant difference between the 2 groups as regards the pattern of calcifications (p=0.001). On the other hand, the mean value of calcification content percentage in cases presented with ACS ranged from 18% ± 8.7% to 35.1 % ± 16 %, while in cases of stable angina, the percentage ranged from 66.4% ± 13.8% to 76.7% ± 16.5%. There were statistically significant differences between both groups only as regards the proximal

coronary segments (p=0.00-0.013), yet the distal showed no significant differences (p=0.3-0.8). The values are listed in table 7.

	Acute coronary syndrome				Stable Angina				Mann-Whitney U test
	N	Mean	±	SD	N	Mean	±	SD	p-value
p-RCA	5	18.0	±	8.7	16	71.1	±	10.7	0.000*
LM	0	NA			8	73.9	±	11.5	NA
p-LAD	2	34.7	±	2.5	22	71.4	±	10.4	0.007*
p-LCx	2	34.7	±	6.1	16	66.4	±	13.8	0.013*
m-RCA	5	26.6		11.2	10	20.2		5.7	0.31
m-LAD	4	26.1		16.3	16	22.4		8.9	0.82
m-LCx	4	29.8		16.4	8	21.7		10.7	0.46
OM 1	0	NA			8	20.6		8.8	0.46

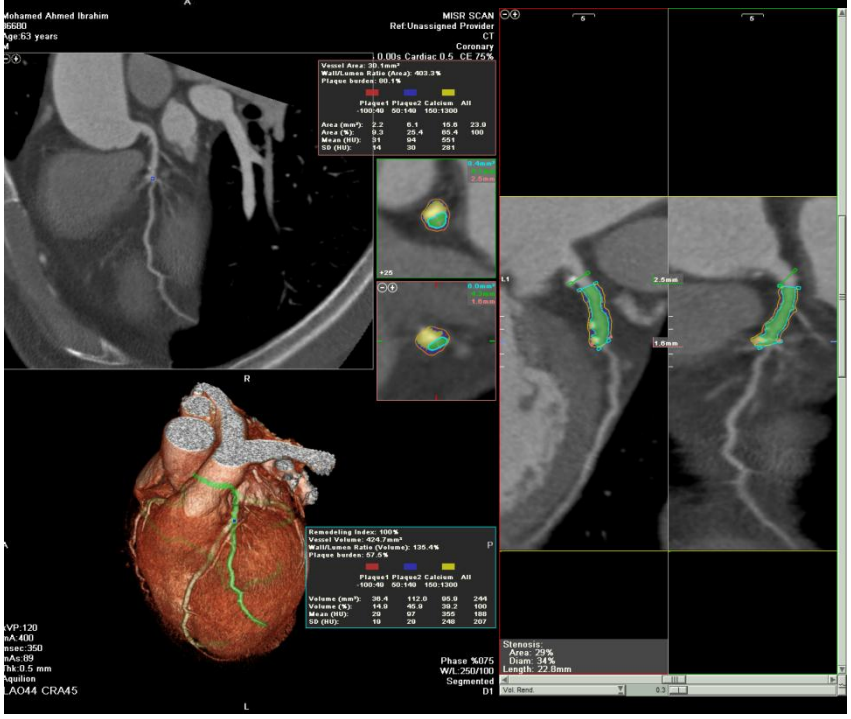
Table (7): Distribution of the mean percentage values of calcification plaque contents of the coronary segments in cases of ACS and SA.

Illustrative cases:

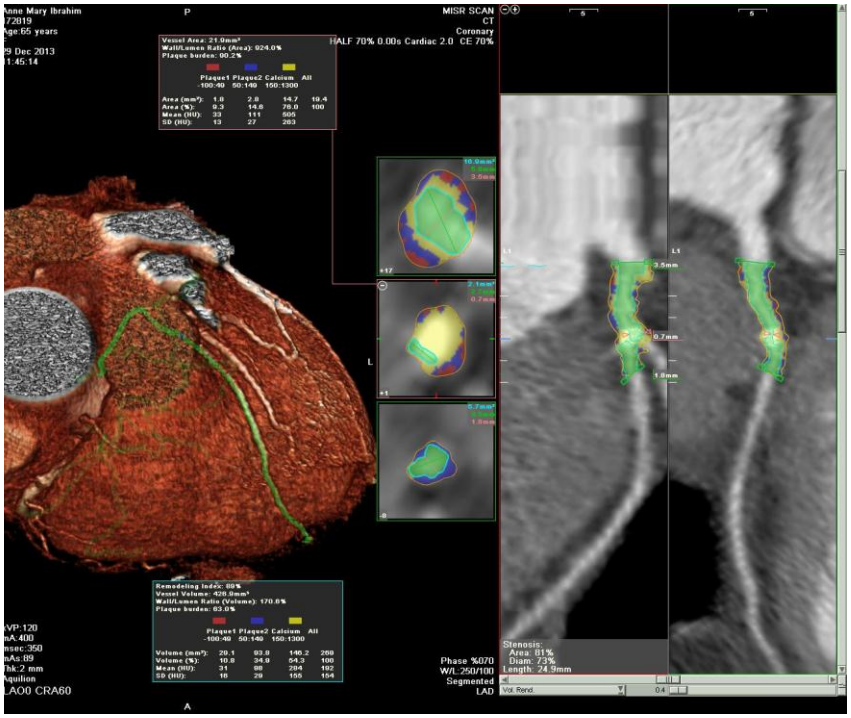


59 years old male patient presented coronary syndrome (ACS) with eleva enzymes and ECG findings characteristi wall infarction, Quantitative MDCT angiography displaying a predominantly at the distal LCx.

40 years old male patient preser with ACS, elevated car enzymes and ECG changes inferior wall infarction. Quantita plaque assessment shows a r calcified plaque with mixed tissue/lipid content of the R segment.



53 years old male pat presented with chest pain, r elevated cardiac enzymes normal ECG (Stable angi Quantitative plaque assessn shows a predominantly calci plaque D1 coronary segment.



65 years old female patient presented with chest pain, non-elevated cardiac enzymes and normal ECG (Stable angina). Quantitative plaque assessment shows an almost entirely calcified plaque of the LAD.

Discussion:

Coronary plaque detection and stenosis quantification: In our study all proximal and middle coronary arterial segment plaques were excellently visualized in both patient groups (ACS and SA) amounting to a total of 134 segments with visualized plaques. This came in agreement with Leber et al. who reported a sensitivity of 84% and a specificity of 91% in the detection of proximal coronary plaques [(11)], also Sun et al, reported higher sensitivity and specificity figures (97.4% & 90.1% respectively) of 64-MDCT for detection of proximal and middle segment coronary plaques as compared to intravascular ultrasound (IVUS) [(10)].

The visualized plaques in cases presented with ACS, showed higher degree of stenosis by area method in comparison to those presented with SA (a mean stenosis percent value ranging between 77.2% and 90.5 % for the earlier and 54.1% - 65.2 % for the latter). These findings agree with a study carried by Schuijf et al, where they showed that patients presented with ACS and abnormal myocardial perfusion imaging results, showed higher degrees of coronary arterial stenosis by virtue of the culprit coronary plaques as compared to patients presented with SA and normal myocardial perfusion imaging [(12)].

Characterization of plaque composition: Our current study takes after several studies that explored the ability of the 64-row MDCT to characterize the coronary arterial plaques according to their composition based on the mean attenuation value of the plaque measured in HU. Schroeder et al reported earlier a density of soft (14±26 HU), fibrous (91±21 HU) and calcified plaques (419±194 HU), suggesting that a density of <50HU should identify soft plaque, density from 50–119 HU should identify dense fibrous plaques, and density >120 HU should identify dense calcified plaques, based on post mortem histopathological comparison of the coronary plaques imaged by CT [(13)].

Based on the aforementioned concept, our study pursued the ability of 64-row MDCT to quantify the different constituents of the coronary plaque using values of -100 – 49 HU for low density/lipid components, 50 – 149 HU for dense/fibrous tissue components, and > 150 HU for calcified components.

Lipid content and "culprit" lesions: The results of our current study came in agreement with the results of studies carried by Rodriguez-Granillo et al and Motowaya et al, as well as the succeeding work of Kitagawa et al who – also using 64 rows MDCT – showed that more non calcified plaques (NCP)/patient were detected in the ACS group than the non-ACS group. These studies showed more NCPs in ACS patients (65 lesions, 3.1±1.2/patient) than in non-ACS patients (163 lesions, 2.0±1.1/patient). Minimum CT density

(24±22 vs. 42 ±29 Hounsfield units [HU], p=0.01). The plaques that were detected more frequently in ACS displayed "vulnerable" characteristics, including overall lower CT density, and presence of adjacent spotty calcium. [14], [15], [16]

Sun et al used a similar software for plaque analysis, to detect plaque composition as compared to the corresponding results of intravascular ultrasound (IVUS). The lesions in the MDCT software tool analysis were accurately detected, as compared to IVUS results; in addition, morphology of the coronary plaques was properly visualized and quantified.[10]

In our study, we were able to identify the morphological criteria of the culprit and non-culprit lesions in cases of ACS and SA, where the overall low density/lipid content percentage of the culprit plaques in the cases presented with ACS (ranging between 15.4% ± 0.8% and 47.7 % ± 19.2 %), was significantly higher than in cases presented with SA (ranging between 7.2% ± 5.5% and 10.3% ± 8.2%).

Soft/fibrous tissue content and "culprit" lesions: In our study, data showed that the soft tissue content percentage of the plaques with attenuation values between 30 – 150 HU, showed higher percentages among cases with ACS (mean values ranged from 15.4% ± 0.8% to 47.7 % ± 19.2) as compared to cases with SA (7.2% ±5.5% to 10.3% ± 8.2%), yet the soft tissue content percentage per se didn't show clear difference between the cases of ACS and those with SA. Rodriguez-Granillo et al observed a converse trend for fibrotic content of culprit lesions associating cases presented with ACS. [14]

Calcification content and coronary plaques: Considering plaque calcifications, our current study showed significant difference between the pattern of calcifications present in cases presented with ACS and those presented with SA, where the prevalent pattern present within the culprit plaques in ACS cases was of the spotty type (92% of all culprit plaques), whereas the prevalent calcification pattern in cases of SA was that of the diffuse type (81%). In addition to calcification pattern/distribution, further assessment of the plaque calcifications in our study, showed – as anticipated – a higher percentage of plaque calcium in cases presented with SA (mean values of plaque calcium content ranged 66.4% ± 13.8% to 76.7% ± 16.5%), in contrast to cases presented with ACS that had lower plaque calcium percentages (18% ± 8.7% to 35.1 % ± 16 %).

Conclusion:

The 64-row MDCT coronary angiography with the aid of semi-automatic plaque quantification tool used in our study showed statistically significant differences as regards the plaque composition, lipid and calcium percentages, calcification pattern, and degree of stenosis. This could provide a new basis for future attempts of risk stratification of patients with coronary artery disease (CAD) especially those liable for developing ACS.

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