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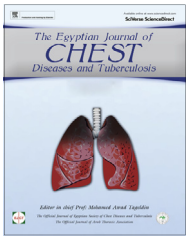

ORIGINAL ARTICLE

Qualitative and Quantitative Coronary Angiography in patients with Acute Coronary Syndrome (ACS)

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KEYWORDS

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Abstract *Background and Aim:* Acute Coronary Syndrome (ACS) encompasses several diseases, previously thought to be separate and defined disease states. In this syndrome, Unstable Angina (UA), Non-ST Elevation Myocardial Infarction (NSTEMI), and ST-Elevation Myocardial Infarctions (STEMI) are all part of this category. The pathogenesis begins with plaque rupture which activates the platelets and coagulation cascade leading to thrombus formation. The thrombus leads to partial or complete coronary artery occlusion leading to various clinical manifestations of ACS.

The aim of the present study is to assess the extent of coronary artery disease and characterizes plaque morphology and lesion severity in patients with ACS in comparison with patients with chronic stable ischemic heart disease.

Subjects and Methods: To achieve this aim, we studied 100 patients with symptomatic coronary artery disease admitted to Mansoura medical Hospital, where they were subjected to full clinical evaluation; 12 lead electrocardiogram, full laboratory investigations and Coronary angiography was done to every patient, then we analyses the results both qualitative (eye ball description of angiographic lesions) and quantitative (computer-based). Those patients were classified into two main groups, the first group of patients were those with ACS (50 patients) as a *test group* while the second one included patients chronic stable ischemic heart disease (50 patients) as a *control group*.

Results: Both groups were comparable and no significant difference was present as regard age, sex, diabetes mellitus, hypertension, smoking, left ventricular function, prior PTCA, prior CHF and angina class while, prior MI more frequent among test group. One hundred, forty-seven lesions (66 in test group and 81 in control group) were available for detailed qualitative angiographic analysis. Out of seven criteria analyzed only presence of lumen *irregularity* and *thrombus* were more frequent among patient who presented with ACS (17 (26%) vs. 2 (2.5%) $p < 0.05$; 9 (13.6%) vs. 0 (0%)

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$p < 0.05$) respectively), and this represents the main finding in the current study. No significant difference was present in Quantitative Coronary angiographic characteristics in both groups.

Conclusion: The qualitative angiographic assessment represents an essential tool in the evaluation and risk stratification of patients with ACS, through the demonstration of the presence of thrombus and lumen irregularity that correlated more with ACS than the other studded criteria. In addition, QCA although added accurate assessment of the degree of luminal narrowing, thus helping in assessment of the severity of the disease.

Introduction

Acute Coronary Syndrome (ACS) encompasses several diseases, previously thought to be separate and defined disease states. In this syndrome, Unstable Angina (UA), Non-ST Elevation Myocardial Infarction (NSTEMI), and ST-Elevation Myocardial Infarctions (STEMI) are all part of this category. The pathogenesis begins with plaque rupture which activates the platelets and coagulation cascade leading to thrombus formation. The thrombus leads to partial or complete coronary artery occlusion leading to various clinical manifestations of ACS. Identification of the coronary endoluminal lesion(s) responsible for ACS has become a central focus of both non-invasive and invasive treatment modalities in patients with coronary heart disease [1].

Since its introduction, conventional coronary angiography in the standard clinical means for depicting the coronary arteries and is ''gold standard'' for diagnosis CAD [2]. Heterogeneity of the composition, distribution and location of atherosclerotic plaque within the native coronary artery results in a unique patterns of stenosis morphology in patients with CAD. These unique atherosclerotic patterns have been used to identify risk factors for procedural outcome and complications after PCI and to assess the risk of recurrent events in patients who present with ACS [3]. Focus on the culprit coronary lesion in patients with ACS allows recognition of the complex plaque and of presence of endoluminal thrombi that are closely associated to the mechanisms of the disease [1].

The vast majority of the clinical catheterization laboratories continue to relay on visual ''eye ball'' estimates of percent diameter stenosis to quantify the severity of the coronary disease. Unfortunately, visual estimates of lesion severity are neither reproducible nor accurate. Because the visual interpretation of coronary angiograms is inherently flowed, numerous computer-assisted, Quantitative Coronary Angiography (QCA) systems have been developed, their common purpose the geometric assessment of epicardial coronary abnormalities [4].

Aim of the work

Coronary heart disease has been extensively studied in the western countries and few data are available about this common disease among Egyptian patients. This study represents the initial angiographic study conducted in our institute. It aims to characterize the angiographic features among Egyptian patients presented with Acute Coronary Syndrome (ACS). In addition, it aims to develop and improve our cine angiographic interpretative skills.

Subjects and methods

Case selection and study population

This is a clinical study that included two main groups of patients with symptomatic ischemic heart disease (a) *group 1*: patients presented with ACS as a test group ($n = 50$, 38 males and 12 females; mean age 53.8 ± 1.1 years) and (b) *group 2*: patients presented by chronic stable angina pectoris as control group ($n = 50$, 41 males and 9 females; mean age 52.8 ± 8.9 years). Both groups were chosen from patients who underwent diagnostic coronary angiography in the period from January, 1, 2005, till December, 31, 2006) in Specialized Medical Hospital (MSH), Mansoura University, Egypt.

Informed consent

After thorough explanation of the technique and possible procedural risks and benefits, all patients signed a written consent for coronary angiography and possibility of intervention either PTCA or emergent CABG.

All patients were subjected to full clinical evaluation; 12 lead electrocardiogram, full laboratory investigations and Coronary angiography was done to every patient, then we analyses the results both qualitative (eye ball description of angiographic lesions) and quantitative (computer-based).

Qualitative Angiographic Analysis

All cine angiograms of both groups were analyzed by two different experienced interventional cardiologists blind for the clinical data of the patients. Reporting on the following twelve characteristics:

1- **Site of the lesion**: Lesion location was specified by the proximal portion of the lesion, even though of sufficient length to extend into a more distal segment.
2- **Number of the lesions**
3- **Restenotic lesion**: Defined as significant coronary stenosis (> 50% diameter of stenosis by QCA) at the site of previous PTCA [5].
4- **Bifurcation lesion**: A lesion that involved two major epicardial coronary arterial branches, the smaller of which was at least of moderate size (> 1.5 mm in diameter) and otherwise would have been surgically bypassed. This branch originated within the stenosis in the main artery and itself had a > 50 % stenosis at its origin [6].
5- **Eccentric lesion**: A stenosis asymmetrically positioned in the vessel in any angiographic projection by visual assessment [7].

6- **Lumen irregularity**: Presence of irregularities or saw tooth appearance on the luminal border of the target lesion [8].
7- **Thrombus**: Presence of an intraluminal filling defect of convex curvature, well separated from the adjacent vessel wall at the site of the target lesion [9].
8- **Total occlusion**: It was defined as total obstruction of epicardial coronary vessel without ante grade flow (TIMI flow grade 0); the distal vessel may or may not have been filled through retrograde or ante grade (bridging) collateral flow [5].
9- **Coronary collateral circulation**: Coronary collaterals are anastomotic connections without an intervening capillary bed between portions of the same coronary artery and between different coronary arteries [10].
10- **Tourtosity of the proximal segment (lesion accessibility)**: It was graded according to the number of significant bends (>45°) in the part of the vessel proximal to the target lesion. It was assessed at least in two perpendicular views. It was graded according the following scale; 0 (none), no significant bend; 1 (mild), presence of single significant bend; 2 (moderate), presence of two significant bends; 3 (severe), the target lesion was distal to three significant bends or more [8].
11- **Angulation of the lesion**: It was the angle formed by the centreline through the lumen proximal to the stenosis and extending beyond it, and a second centreline in the straight portion of the artery distal to the stenosis. It was graded into; 0 (non-angulated lesion), if the angle is zero i.e., the lesion was straight; 1 (mild-angulated), if it was <45°; 2 (moderately-angulated), if the angle was >45° but < 90°, and 3 (extremely-angulated), if the angle was >90° [8].
12- **Lesion calcification**: It was defined as fixed radiopaque densities seen in the area of the stenosis, and it was graded as minimal when they were difficult to detect, moderate when they were easy to detect, and heavy when they were of spine density. The extent of calcification was coded as follows; 0 (non-calcified lesion); 1 (mildly-calcified), calcification occupied less than one third of the length of the lesion; 2(moderately-calcified), calcification occupied between one third and two thirds of the lesion length; 3(severely-calcified), at least two thirds of the lesion length is calcified [11].

Quantitative Coronary Angiography (QCA) Analysis

Steps of QCA. The radiographic equipment used was AXIOM ARTIS FC/BC, AXA 4, Siemens, Germany with software; DICOM compliant.

QCA analysis includes many steps which include; selecting a scene/image, calibration, selecting the diseased segment of the artery, artery contour detection, performing analysis, and final reporting in two pages.

Of many variables displayed we selected the following variables; Minimal Luminal Diameter (MLD) [mm]: The minimum vessel diameter at the position of the most severe stenosis [12]. (% Diameter Stenosis) (%DS) The percentage of the diameter of the most severe stenosis compared with the reference diameter; stenosis diameter/reference diameter × 100% [13]. Lesion length [mm]: Length of the analyzed vessel segment [12]. *and* Reference Diameter (RD): [mm]: Diameter of the vessel at the reference point [13].

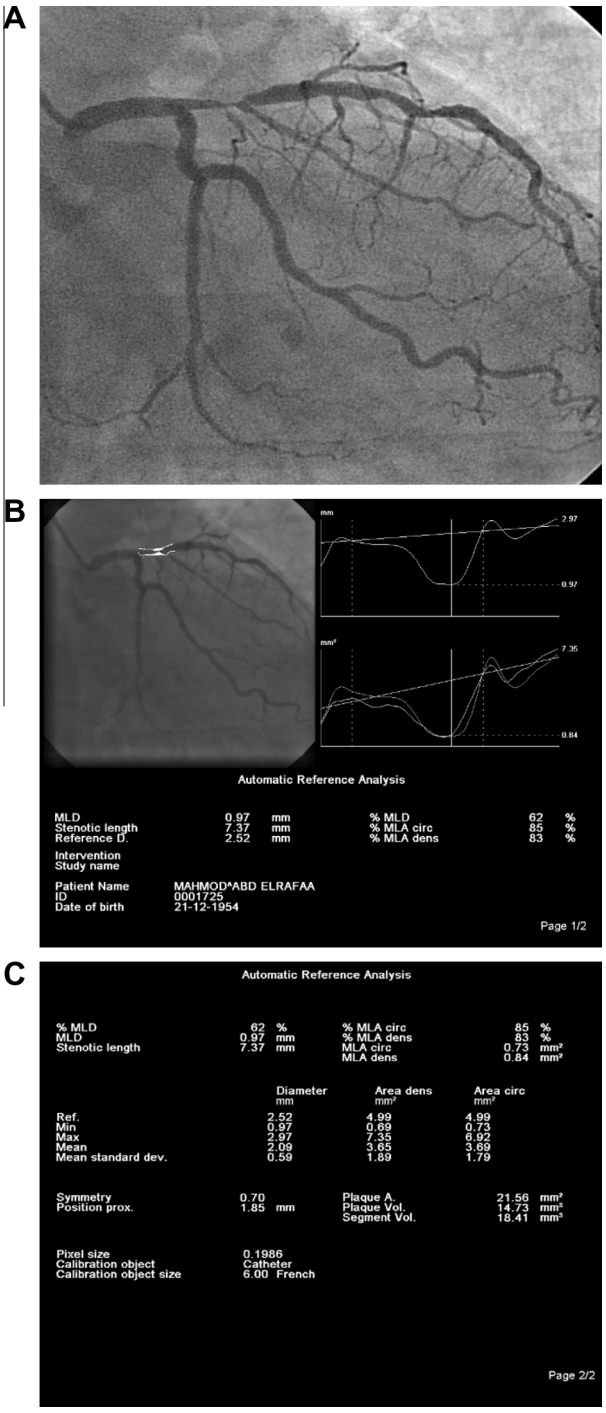

Figure 1 Case No.4 (test group) male patient ages 52 years old, diabetic, hypertensive, dyslipedemic and smoker (A) left coronary angiogram in RAO CAUDAL view, the LAD artery showing proximal critical irregular eccentric bifurcational lesion including S1& D1 with good distal run off (TIMI III). (B) and (C) technique and print out of QCA data of the target lesion.

Fig. 1 shows how QCA is done for illustrative case and finally displayed.

Statistical analysis

Categorical variables (such as sex, lesion type, lesion location, nominal lesion characteristics, etc.) were presented as absolute numbers and percentage. Continuous variables (such as age, reference vessel diameter, minimal luminal diameter, % diameter stenosis, etc.) were expressed as mean value ± Standard Deviation (SD). Differences between groups were evaluated by using adjusted Chi-square test for categorical variables and two-tailed student *t*-test or Man–Whitney test for continuous variables. Probability values (*P* value) < 0.05 was considered statistically significant. *(Data were analyzed with SPSS software computer package version 10.)*.

Results

Table 1 summarize the base line clinical characteristics of both groups, both groups were comparable and no significant difference was present as regard sex, diabetes mellitus, hypertension, smoking, prior PTCA, prior CHF and angina class WHILE, prior MI more frequent among test group (*P* value 0.023).

Table 2 summarize the Qualitative coronary angiographic characteristics of both groups, both groups were comparable and no significant difference was present as regard site of lesions, number of lesions, calcification, total occlusion and collateral EXCEPT, thrombus, and lumen irregularity more frequent among ACS group.

Table 3 summarize the QCA in LAD, LCX, RCA and OM arteries of both groups, both groups were comparable and no significant difference was present.

Discussion

The main finding in this study is that the presence of thrombus and lumen irregularity is significantly common among patients presented with ACS when compared with patients with chronic stable coronary artery disease.

Table 1 Baseline clinical characteristics of both groups.

Characteristics	ACS group ($n = 50$)	Stable angina group ($n = 50$)	*P* value
Gender			
Male (n, %)	38 (76%)	41 (82%)	0.461
Female (n, %)	12 (24%)	9 (18%)	
Diabetes (n, %)	26 (52%)	23 (46%)	0.458
Hypercholesterolemia (n, %)	29 (58%)	24 (57%)	0.934
Smoking current (n, %)	22 (44%)	15 (30%)	0.243
Ex-smoker (n, %)	10 (20%)	9 (18%)	
Non-smoker (n, %)	18 (36%)	26 (52%)	
Hypertension (n, %)	34 (68%)	39 (78%)	0.260
Prior MI (n, %)	24 (48%)	13 (26%)	0.023
Prior CHF (n, %)	5 (10%)	2 (4%)	0.240
Angina Class 0 (n, %)	0 (0%)	3 (6%)	0.934
1 (n, %)	0 (0%)	25 (50%)	
2 (n, %)	22 (44%)	22 (44%)	
3 (n, %)	28 (56%)	0 (0%)	
Prior PTCA (n, %)	1 (2%)	0 (0%)	0.315

Table 2 Qualitative coronary angiographic characteristics.

Characteristics	ACS group ($n = 50$)	Stable angina group ($n = 50$)	*P* value
Site of lesions:			
L. main (n, %)	3 (4.5%)	3 (3.7%)	–
LAD (n, %)	28 (42.4%)	30 (37%)	
Diagonal (n, %)	2 (3%)	0 (0%)	
LCX (n, %)	4 (6%)	13 (16%)	
OM (n, %)	5 (7.6%)	7 (8.6%)	
RCA (n, %)	23 (34.8%)	26 (32%)	
PDA (n, %)	1 (1.5%)	1 (1.2%)	
PLVB (n, %)	0 (0%)	1 (1.2%)	
Number of lesions:			
One (n, %)	27 (50%)	23 (28.4%)	0.858
Two (n, %)	16 (24.2%)	20 (24.7%)	
Three (n, %)	5 (7.6%)	5 (6.2%)	
Four (n, %)	2 (3%)	2 (2.5%)	
Presence of thrombus (n, %)	9 (13.6%)	0 (0%)	0.002
Presence of irregularity (n, %)	17 (26%)	2 (2.5%)	0.003
Calcification (n, %)	8 (12.12%)	11 (13.6%)	0.444
Total occlusion (n, %)	10 (15.2%)	2 (2.5%)	0.240
Collateral (n, %)	2 (4%)	4 (5%)	0.400

Table 3 Quantitative coronary angiographic characteristics in both groups.

Characteristics	ACS group (66 lesions)	Stable angina group (81 lesions)	*P* value
	Mean ± SD	Mean ± SD	
LAD:			
RD	2.9 ± 0.69	2.9 ± 1.0	0.877
MLD	1.46 ± 0.69	1.31 ± 0.54	
%DS	50.8 ± 13.67	52.2 ± 11.6	
Length	8.07 ± 3.4	10.48 ± 4.47	
LCX:			
RD	3.2 ± 0.8	2.7 ± 0.9	0.367
MLD	1.8 ± 0.7	1.4 ± 0.5	
%DS	44.5 ± 7.7	51.7 ± 15.2	
Length	7.3 ± 2.95	12.5 ± 8.2	
LCX:			
RD	2.9 ± 0.9	3.2 ± 1.3	0.341
MLD	1.6 ± 0.8	1.7 ± 0.7	
%DS	50.5 ± 17.2	55.7 ± 19.0	
Length	10.3 ± 5.7	12.6 ± 8.3	
OM:			
RD	2.7 ± 1.1	2.5 ± 0.4	0.689
MLD	1.5 ± 1.0	1.5 ± 0.5	
%DS	53 ± 16.2	39.9 ± 15.9	
Length	13.95 ± 8.5	12.3 ± 13.9	

Qualitative coronary angiographic analysis

Since its introduction, conventional coronary angiography in the standard clinical means for depicting the coronary arteries and is "gold standard" for diagnosis CAD [2].

Heterogeneity of the composition, distribution and location of atherosclerotic plaque within the native coronary artery re-

sults in a unique patterns of stenosis morphology in patients with CAD. These unique atherosclerotic patterns have been used to identify risk factors for procedural outcome and complications after PCI and to assess the risk of recurrent events in patients who present with ACS [3].

Assessment of severity of atherosclerotic coronary affection may be more usefully based on the presence of one or more specific morphologic features rather than use of composite scoring system, like that established by Joint Committee of ACC/AHA [14]. Myler et al. [5] stated that it is better to specify than to classify after use of ACC/AHA criteria in large series of patients who underwent PCI.

Characterization of plaque morphology can provide useful information beyond those generally yielded by the more traditional methods of interpretation of coronary angiograms based on assessment of severity of stenoses and number of diseased vessels. Focus on the culprit coronary lesion in acute myocardial infarction and in unstable angina allows recognition of the complex plaque and of presence of endoluminal thrombi that are closely associated to the mechanisms of the disease [1].

Despite computer assisted QCA methods estimates the extent of geometric obstruction and to lesser extent functional severity of atherosclerotic lesions, in an absolutely accurate and reproducible manner, many fail to predict the behavior of the coronary lesions. To more fully characterize an atherosclerotic lesion, Qualitative, morphologic lesion descriptors must be analyzed along with Quantitative measures. Numerous studies have suggested that qualitative descriptors of lesion severity are potent predictors of outcome, independent of the degree of geometric obstruction [11–13].

One hundred, forty-seven lesions (66 in test group and 81 in control group) were available for detailed qualitative analysis. Out of twelve criteria analyzed only presence of lumen *irregularity* and *thrombus* were more frequent among patient who presented with ACS (17 (26%) vs. 2(2.5%) $p < 0.05$; 9 (13.6%) vs. 0 (0%) $p < 0.05$) respectively), and this represents the main finding in the current study.

Lesion irregularity

Lesion irregularity, including lesions with ulceration, a ''sawtooth pattern'', or an intimal flap, suggest a friable surface and correlated pathologically with plaque fissuring, rupture and platelet and fibrin aggregation [15]. Out of 66 lesions among patients with ACS, 17 (34%) have irregular lumen compared to 2 out of 81 lesions in stable angina group ($p < 0.05$).

Our results are *in agreement with* that reported in many studies [15–17]. Who reported that complex, irregular plaques have been associated with unstable coronary syndromes.

On the other hand, the reported incidence of irregular lesions among patients with stable angina pectoris is 2 out of 81 lesions (2.5%). Waters et al. [18], reported that irregular lesion is rarely seen in patient with stable angina pectoris; ranging from 1.5% to 3.5%.

Thrombus

Over the past decades, the view has evolved that ACS are caused by plaque rupture and formation of platelet thrombus. Coronary thrombosis develops on a plaque that undergoes either erosion or plaque rupture [19]. Rupture of the fibrous cap of the plaque results in exposure of the deep layers, which is extremely thrombogenic because it contains a large amount of tissue factors [20].

A full sized thrombus can easily develop consisting of platelets, fibrin and red blood corpuscles that may be sub occlusive or totally occlusive [21]. There is at least a transient total or subtotal coronary occlusion in all cases of STEMI. STEMI are thought to differ from NSTEMI by more stable platelet thrombi causing more prolonged and/or severe ischemia, leading to more extensive tissue necrosis. The greater platelet stability in STEMI is attributed to more severe or extensive plaque rupture [22].

NSTEMI are due to less extensive, less stable platelet thrombi that cause less severe, less extensive ischemia and/or infarction. However, the occlusive thrombi causing STEMI contain more fibrin than thrombi found in the NSTEMI that are characterized by more platelet and less fibrin. The higher fibrin content of thrombi causing STEMI explains their great stability. Furthermore, this higher fibrin content suggests that the coagulation cascade is activated to greater degree during STEMI than during NSTEMI, in which platelets play a more dominant role [23].

Our study revealed that angiographically detected thrombus reported exclusively among patients presented with ACS (9 lesions containing thrombi out of 66 lesions (13.6%) compared to 0% among patients with stable angina pectoris; $P < 0.05$).

This finding is in accordance with that reported with that reported by Dangas et al. [24] who reported that unstable angina pectoris is associated with intracoronary thrombus.

The reported incidence of thrombus in previous study ranged from 35% to 58%.

Incidence in current study seems to be lower than reported in the previous studies; this lower incidence could be explained by that *our institute protocol is to defer coronary angiography after medical stabilization of the patients with ACS*.

Quantitative coronary angiographic analysis

Despite enhanced image acquisition and display, the basic analysis of coronary arteriograms has generally remained unchanged. The vast majority of the clinical catheterization laboratories continue to relay on visual ''eye ball'' estimates of percent diameter stenosis to quantify the severity of the coronary disease. Unfortunately, visual estimates of lesion severity are neither reproducible nor accurate [4].

Because the visual interpretation of coronary angiograms is inherently flowed, numerous computer-assisted, Quantitative Coronary Angiography (QCA) systems have been developed, their common purpose the geometric assessment of epicardial coronary abnormalities [4].

Although QCA appears to substantially improve reproducibility and accuracy, assessment of the lesion dimension, especially percent diameter stenosis, does not predict the functional significance of the coronary lesion. Great effort has been devoted to developing methods that predict the physiologic impact of an obstruction [25,26].

Angiographic methods for estimating the significance of a stenosis are based on either extrapolation from lesion or on independent measurement of flow reserve [27].

One hundred, forty-seven lesion in 100 patients with symptomatic obstructive CAD, were available for complete QCA analysis, for each atherosclerotic lesion; Reference Diameter (RD), Minimal Lumen Diameter (MLD), Percent Diameter Stenosis (DS%),and shoulder to shoulder lesion length in diameter were calculated using computer based QCA (AXIOM ARTIS FC/BC, AXA 4, Siemens, Germany).

Both groups of patients included in this study were matched as regard vessel RD, MLD, % DS and lesion length. Fifty-eight lesions (40%) were located in the left anterior descending artery; RD in the current study was 2.9 ± 0.69 mm, it seems to be much lower than that reported by Dodge et al. [28], who reported 3.7 ± 0.4 mm. Seventeen lesions (12%) were located in the Left Circumflex (LCx) coronary artery; with average RD was 2.95 ± 0.8 mm, also it lower than reported by Dodge et al. [28], who reported 3.4 ± 0.5 mm for non dominant LCx vs. 4.2 ± 0.6 for dominant LCx. Thirty-three percent of lesions (49 lesions) were in the dominant RCA, with average RD was 3.0 mm which is much lower than reported in previous study by Dodge et al. [28] who reported 3.9 ± 0.6 mm for dominant RCA.

This difference in diameter of reference segment in the current study and that reported in literature *can be explain by; first*, patients included in this study have symptomatic obstructive CAD, while the published data were for normal coronary arteries, *second*, by the fact that coronary angiography is ''a luminogram'' in which stenosis severity is evaluated by comparison to adjacent ''reference'' segment that is presumed to be free of disease, *third*, large percentage of diabetic patients in our study. *In fact, both Intravascular Ultrasound (IVUS)* [29] *and pathological examination* [30] *shows that a segment that appears smooth on angiography may harbor substantial plaque.*

In overall conclusion, the qualitative angiographic assessment represents an added tool in the evaluation and risk stratification of patients with ACS, through the demonstration of thrombus formation and lumen irregularity that correlated more with ACS than the other studded criteria. On the other hand, QCA although added accurate assessment of the degree of luminal narrowing, thus helping in assessment of the severity of the disease, it did not correlate with the presence of ACS.

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