

Troponin Positive Acute Coronary Syndrome with and without Significant Stenosis on Coronary Angiography

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ABSTRACT:

BACKGROUND:

Occasionally, coronary arteries without significant stenosis are observed during invasive treatment of acute coronary syndrome (ACS).

OBJECTIVE:

The aim was to study the frequency and to determine the most predictive factors of Troponin positive ACS without significant Stenosis on angiography.

METHODS:

The study involved one hundred twenty four patients admitted with Troponin positive ACS who underwent cardiac catheterization during hospitalization. The primary end-point was the estimation of coronary arteries without significant stenosis, and the secondary end-point was analysis of the most predisposing factors. In evaluating the primary end-point, the patients were divided into two groups according to the presence of ST elevation myocardial infarction (STEMI) or not. Also the patient who has no significant coronary artery Stenosis (< 50%) was subdivided to two groups:

a- Myocardial Infarction with No critical lesion in Coronary angiogram (MINC)

b-Normal coronary angiogram

RESULTS:

Overall, 20 patients (16%) had coronary arteries without significant lesions, from which 8 patients (6.4%) had MINC and 12 patients (9.6%) had normal coronary angiogram. The predictors were: female sex ($P=0.008$), age <45 years ($P=0.001$), and the absence of: diabetes ($P=<0.001$), hypertension ($P=0.005$) and absence of ST-segment elevation ($P=0.001$). Furthermore absence of regional wall motion abnormality (RWMA) is considered as another predictors for non-significant coronary artery lesion ($P=0.008$). Also the angiographic analysis of all lesions revealed that single vessels CAD are the commonest finding in Group I patients ($P= 0.02$). We further analyzed a suspicious angiographic lesions by using QCA {18 lesions (14.5%)} and FFR {6 lesions (4.8%)} technique.

CONCLUSION:

Overall, patients with Troponin positive ACS had non- significant coronary artery Stenosis on angiography, and female sex, age <45 years and the absence of diabetes, hypertension, ST- segment elevation or RWMA were all associated with coronary angiography showing no significant stenosis.

KEYWORD: troponin, acute coronary syndrome, angiography.

INTRODUCTION:

The rupture of an atheromatous plaque in association with a variable degree of thrombosis, in relation to a local inflammatory process, is the underlying origin of acute coronary syndrome⁽¹⁾. In patients who have acute coronary syndromes, an elevated level of cardiac Troponin (suggestive of myocardial necrosis) is a well-known risk factor for

fatal events⁽²⁾. Although acute myocardial infarction is generally associated with obstructive coronary artery disease, between 8% and 12% of patients have normal coronary arteries^(3, 4&5). However, the characterization of and prognosis for patients who present with acute typical anginal pain and elevated ischemic markers—but without critical coronary artery stenosis—remain uncertain⁽⁶⁾. Patients with STEMI and normal coronary arteries tend to be young, with relatively few

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coronary risk factors. Usually, they have no history of angina pectoris before the infarction. The infarction in these patients is usually not preceded by any prodrome, but the clinical, laboratory, and electrocardiographic features of STEMI are otherwise indistinguishable from those present in the overwhelming majority of patients with STEMI who have classic obstructive atherosclerotic coronary artery disease⁽⁷⁾. The long-term outlook for patients who have survived a STEMI with angiographically normal coronary vessels on arteriography appears brighter than for patients with STEMI and obstructive coronary artery disease⁽⁸⁾.

PATIENTS AND METHODS:

Data collection: The study included one hundred twenty four consecutive patients, who attended Ibn Al-Betar, Al-Naseria and Iraqi centers for cardiac disease for chest pain and were admitted with AMI including both ST-elevation myocardial infarction (STEMI) and non-STEMI between April, 2012 and January, 2013. The following criteria had to be met for inclusion in the study:

1) Satisfied the criteria for AMI { typical rise and fall in cardiac biomarkers (Troponin) with at least one value above the 99th percentile of the upper reference limit together with evidence of myocardial ischemia with at least one of the following:

Symptoms of ischemia, ECG changes indicative of new ischemia (new ST-T changes or new left bundle branch block, development of pathologic Q wave)⁽⁷⁾.}

2) Elevated troponin Tor I in serial measurements on arrival at hospital and/or 8-12 hours after the onset of pain.

3) Cardiac catheterization and coronary angiography were performed during admission.

Patients were classified into two groups according to the presence or absence of significant coronary artery stenosis as follows:

Group I ($\geq 50\%$ diameter Stenosis)

Group II ($< 50\%$ diameter Stenosis), which subdivided in to:

Group II-a {Myocardial infarction with no critical lesion in coronary angiogram (MINC)}

Group II-b {normal coronary angiogram}

The following patients were excluded from the study:

1// Patients who underwent thrombolysis. 2// Patients with history of renal failure. 3// Patients who underwent coronary angiography previously.

The two different Troponin tests were used during the study: COBAS h 232 roche (quantitative cTnT upper limit of normal, 0.5 ng/mL)

DIAQUICK cardiac combo cassette (qualitative cTnI upper limit of normal, 1.0 ng/mL).

Coronary angiography: Conventional coronary angiography was performed in a standard manner. Standard multiple projections were recorded for the left and right coronary arteries, following the insertion of the arterial sheath. We further analyzed suspicious angiographic lesions by using QCA and FFR technique; we enrolled 18 lesions from all 124 analyzed patients to QCA analysis and 6 lesions to FFR analysis.

Statistical analysis: Continuous variables were expressed as mean \pm SD. Comparisons for continuous variables were performed using chi-square test, a p value < 0.05 was considered statistically significant.

RESULTS:

The clinical characteristics are described in (Table 1) and the ECG and echocardiographic findings are described in (Table 2).

Coronary Angiographic Analysis: After screening the angiographic data for the 124 patients presenting with AMI, a total of 20 consecutive patients (10 men and 10 women) fulfilled the angiographic criteria and were included in the final analysis of Group II. The angiographic finding of Troponin positive patients with ACS are shown in (Figure 1). Angiographic results of 124 patients enrolled in the study revealed that 104 (83.8%; $P=0.04$) patients had significant CAD ($\geq 50\%$) {Group I} , 8 (6.4% ; $P= <0.01$) had a non- significant CAD ($< 50\%$) {Group II-a } and 12(9.6% ; $P= <0.01$) had a normal coronary angiogram{Group II-b}.Then we further sub classify the two groups according to the ECG finding (Table 3) (Figure 2). 60(48.3%) of patients had ST elevation myocardial infarction (STEMI) 64 (51.7%) of patients had (Non- STEMI) , the angiographic analysis revealed that patients with Non- STEMI had more non-significant CAD {9.3% versus 3.3% ; $P= <0.01$ } and normal coronaries { 15.6% versus 3.3% ; $P= <0.01$ } than patients with STEMI. Also the angiographic analysis of all lesions revealed that

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single vessels CAD are the commonest finding in Group I patients {50% of STEMI and 34.4% of Non- STEMI; P= 0.02}.

Quantitative coronary angiography (QCA) and fractional flow reserve (FFR) subgroup

We further analyzed suspicious angiographic lesions to decrease or even eliminate the bias in our study regarding assessment the degree of Stenosis which is difficult to be assessed visually by using

QCA and FFR technique (Table 4) (Figure 3). We totally estimate 24 (19.3%) lesions from all 124 patients included in our study and enrolled 18 lesions (14.5%) to QCA analysis which revealed that 10 lesions (55.6% ; P= 0.05) had significant CAD and 6 lesions (4.8%) to FFR analysis which revealed that 4(66.7% ; P= 0.08) patients had significant CAD .

Table 1: Clinical characteristics of the patients.

Variable	Group I (n=104)	Group II (n=20)			P value
		Group II-a (n=8)	Group II-b (n=12)	Total (n=20)	
Age(yrs)	55.1 ± 12	43.5 ± 9	45 ± 9.8	44 ± 7	0.001
Female No.(%)	28(26.9%)	2(25%)	8(66.6%)	10 (50%)	0.008
Male No.(%)	76(73%)	6(75%)	4(33.3%)	10 (50%)	0.008
Risk factor					
Diabetes No.(%)	42(40.3)	2(25%)	2(16.6%)	4 (20%)	< 0.001
Hypertension No.(%)	54(51.9%)	0(0%)	4(33.3%)	4 (20%)	0.005
Smoking(%)	38(36.5%)	4(50%)	3(25%)	7 (35%)	0.008
Hyperlipidemia No.(%)	4(3.8%)	0(0%)	0(0%)	0 (0%)	0.123
Family history No.(%)	12(11.5%)	0(0%)	0(0%)	0 (0%)	0.018
BMI(kg/m ²)	27 ± 3	24.2 ± 3	25.1 ± 3	24.7 ± 3	0.668
Chest pain					
Typical No.(%)	96(92.3%)	8(100%)	4(33.3%)	12(60%)	0.001
Atypical No.(%)	8(7.6%)	0(0%)	8(66.6%)	8 (40%)	0.001

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Table 2: Distribution of ECG and Echocardiographic data according to study group.

Variable	Group I (n=104)	Group II (n=20)			P value
		Group II-a (n=8)	Group II-b (n=12)	Total (n=20)	
ECG findings					
ST elevation	56(53.8%)	2(25%)	2(16.6%)	4(20%)	0.001
ST depression	38(36.5%)	4(50%)	6(50%)	10(50%)	0.200
LBBB	4(3.8%)	0(0%)	0(0%)	0(0%)	0.875
Normal	6(5.7%)	6(75%)	8(66.6%)	14(70%)	0.123
Echocardiographic findings					
RWMA	88(84.6%)	2(25%)	6(50%)	8(40%)	0.008
LV EF (%)	50 ± 12	55 ± 12	63 ± 12	59 ± 12	0.400

Table 3: Angiographic finding of Troponin positive Patients with Acute Coronary Syndrome (ACS)

Angiographic finding	STEMI (n=60)	Non STEMI (n=64)	All patients (n=124)	P value
Group I Significant CAD (%)	56(93.3%)	48(75%)	104(83.8%)	0.04
Left main CAD (%)	2(3.3%)	6(9.4%)	8(6.5%)	0.08
Three-vessels CAD (%)	8(13.3%)	10(15.6%)	18(14.5%)	0.06
Two-vessels CAD (%)	16(26.7%)	10(15.6%)	26(20.9%)	0.12
Single-vessel CAD (%)	30(50%)	22(34.4%)	52(41.9%)	0.02
Group II-a Non significant CAD (%)	2(3.3%)	6(9.3%)	8(6.4%)	<0.01
Group II-b Normal coronaries (%)	2(3.3%)	10(15.6%)	12(9.6%)	0.01

Table 4: Analysis of suspicious coronary angiographic lesions by QCA and FFR.

Parameters	Significant CAD(%)	Non significant CAD(%)	Total (n = 124)	P value
Quantitative coronary angiography (QCA)	10 (55.6%)	8 (44.4%)	18(14.5%)	0.05
Fractional Flow Reserve (FFR)	4 (66.7%)	2 (33.3%)	6 (4.8%)	0.08

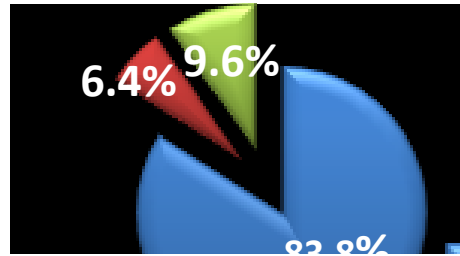


Figure 1: Coronary angiographic finding of Troponin positive ACS.

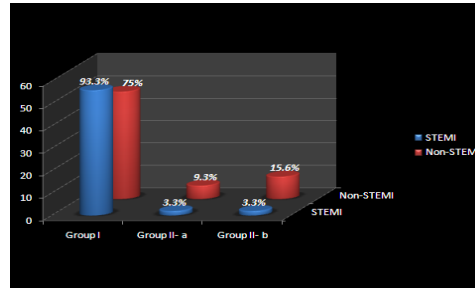


Figure 2: Angiographic analysis according to ECG finding (STEMI and Non-STEMI).

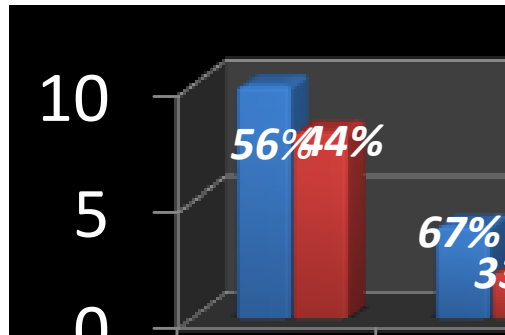


Figure 3: Analysis of suspicious coronary angiographic lesions by QCA and FFR.

DISCUSSION:

Patients who display both acute coronary syndrome and elevation of ischemic markers suggestive of myocardial damage are at high risk of fatal events⁽⁶⁾, but in some cases angiography reveals no critical stenosis. In our study, after we safely excluded other possible causes of a rise in ischemic markers, we found that 16% of the patients with Troponin positive ACS lacked significant coronary stenosis according to the coronary angiogram procedure performed during the initial hospital admission.

The current study demonstrated that the prevalence of MINC(Myocardial Infarction with No Critical lesion), was approximately 6.4% ,while it was approximately 9.6% in a patients with Troponin

positive ACS and normal coronary angiogram .

Comparative previous studies:

Our study shows that a majority of patients with elevated cTn-I or cTn-T have significant coronary artery disease; these results are consistent with previous study by Almeda et al which showing that patients with elevated troponin levels had a higher prevalence of angiographically significant coronary artery Stenosis⁽⁹⁾.

Predictive factors of AMI with Normal Coronary Arteries:

In our study we found that female sex was the variable most strongly associated with absence of significant coronary artery Stenosis and these results are consistent with Alejandro et al study in Valencia, Spain⁽¹⁰⁾.

Regarding other associated factors was age less than 45 years while in Alejandro et al study the age was less than 55 years. Other risk factors including absence of diabetes and absence of hypertension are consistent with Alejandro et al study⁽¹⁰⁾.

Regarding ST changes we found significant variability in the absence of ST elevation and Q wave, these results was similar to the results of Hubertus et al study in Bad Berka, Germany⁽¹¹⁾.

comparative angiographic finding with other studies: The current study reveal that 16% of the patients with acute myocardial infarction lacked significant coronary stenosis according to the coronary angiogram procedure performed during the initial hospital admission, these percentage was higher than of the results of both Shi Hyun et al study (8.2%) in Kwangju, Korea and Hubertus et al study (9%), but it is more consistent with Luis Gruberg et al study (14%) in Haifa^(11, 12).

In our study we found that 15.6% of the patients with Non-STEMI had normal coronary angiogram, these results was higher than the results of Alejandro et al study which found (13%) with normal coronaries⁽¹⁰⁾.

Regarding angiographic finding of significant CAD our study results are consistent with results from Luis Gruberg et al study [single vessel CAD (41.9% versus 38%), two vessels CAD (20.9% versus 24%) and left main and/or three vessels CAD (21% versus 24%)]⁽¹²⁾.

Limitations: The present study had several limitations. First, as the primary objective was to analyze the variables predictive of coronary arteries without significant Stenosis, patients were excluded with a prior documented history of coronary artery Stenosis. Second, catheterization was indicated according to the judgment of the attending cardiologist. Third, the data was collected from patients admitted to the intensive CCU only, and just the patients who underwent angiography were evaluated, thus a selection bias relating to the decision to perform angiography may have influenced the results.

Finally, angiographic data were largely based on operator description, which are subject to inter-observer descriptive variability. All these factors might have influenced the proportion of patients whose coronary angiogram showed no significant stenosis.

CONCLUSION:

Patients with Troponin positive ACS could be presented with non-significant coronary artery Stenosis on angiography (16%), and all the

following factors : female sex, younger patients (age less than 45 years), non diabetic, normotensive, and absence of ST- segment elevation or echocardiographic evidence of RWMA were all consider as predictive factors for such presentation .

REFERENCES:

1. Libby P. Current concepts of the pathogenesis of the acute coronary syndromes. *Circulation*. 2001;104:365-72.
2. Heidenreich PA, Alloggiamento T, Melsop K, McDonald KM, Go AS, Hlatky MA. The prognostic value of troponin in patients with non-ST elevation acute coronary syndromes: a meta-analysis. *J Am Coll Cardiol* 2001;38:478–85. [PubMed]
3. Maehara A, Mintz GS, Bui AB, Walter OR, Castagna MT, Canos D, et al. Morphologic and angiographic features of coronary plaque rupture detected by intravascular ultrasound. *J Am Coll Cardiol*. 2002;40:904-10.
4. Topol EJ, Nissen SE. Our preoccupation with coronary luminology: the dissociation between clinical and angiographic findings in ischemic heart disease. *Circulation*. 1995;92: 2333-42.
5. Humphries KH, Pu A, Gao M, Carere RG, Pilote L. Angina with “normal” coronary arteries: Sex differences in outcomes. *Am Heart J*. 2008;155:375-81.
6. Dokainish H, Pillai M, Murphy SA, DiBattiste PM, Schweiger MJ, Lotfi A, et al. Prognostic implications of elevated troponin in patients with suspected acute coronary syndrome but no critical epicardial coronary disease: a TACTICS-TIMI-18 substudy [published erratum appears in *J Am Coll Cardiol* 2005;45:1911. *J Am Coll Cardiol* 2005;45:19–24. [PubMed]
7. Robert O. Bonow, MD. Myocardial Infarction with Angiographically Normal Coronary Vessels, Braunwald’s heart disease: a text book of cardiovascular medicine. Ninth edition, 4-2436-8089-0-978, 2012.
8. Terefe YG, Niraj A, Pradhan J, Kondur A, Afonso L. Myocardial infarction with angiographically normal coronary arteries in the contemporary era. *Coron Artery Dis* 2007;18:621-26.

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9. Almeda FQ, Calvin JE, Parrillo JE, et al. Prevalence of angiographically significant stenosis in patients with chest pain and an elevated troponin I level and normal creatine kinase and creatine kinase-MB levels. *Am J Cardiol* 2001;87:1286–89.
10. Alejandro Cortell, Juan Sanchis, Vicente Bodí, Julio Núñez, Luis Mainar, Mauricio Pellicer, Gema Miñana, Enrique Santas, Eloy Domínguez, Patricia Palau, and Ángel Llácer. Non-ST-Elevation Acute Myocardial Infarction With Normal Coronary Arteries: Predictors and Prognosis, Original article. *Rev Esp Cardiol*. 2009;62:1260-66
11. Hubertus von Korn, MD, Volker Graefe, MD, Marc-Alexander Ohlow, MD, Jiangtao Yu, MD, Burkhard Huegl, MD, Andreas Wagner, MD, Stefan Gruene, MD, and Bernward Lauer, MD. Acute Coronary Syndrome without Significant Stenosis on Angiography Characteristics and Prognosis, *Tex Heart Inst J*. 2008; 35:406–12.
12. Luis Gruberg, MD, Doron Sudarsky, MD, Arthur Kerner, MD, Haim Hammerman, MD, Michael Kapeliovich, MD, Rafael Beyar, MD, DSc. Troponin-Positive, CK-MB-Negative Acute Myocardial Infarction: Clinical, Electrocardiographic and Angiographic Characteristics, *J Invasive Cardiology* 2008;20:125–28.