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C-Reactive Protein to Albumin Ratio Versus Coronary Artery Ectasia as Predictors of No-reflow After Primary Percutaneous Coronary Intervention for Patients Presenting with ST Segment Elevation Myocardial Infarction

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Aims: to assess and compare the significance of C-reactive protein Albumin ratio (CAR) versus coronary artery ectasia (CAE) as predictors of no-reflow phenomenon.
Methods: This study was conducted on 90 ST segment elevation myocardial infarction patients treated with primary percutaneous coronary intervention (PPCI) within 24 hours of presentation at cardiovascular medicine department Tanta university hospitals in Gharbia Governorate, Egypt. This is a prospective study and data collection was done within 12 months started from June 2018. Patients were divided into two groups according to the post primary PCI thrombolysis in myocardial infarction (TIMI) flow score. Group I (Case group), patients with no-reflow phenomenon TIMI 0-1 flow post primary PCI. Group II (Control group) with TIMI flow ≥ 2 after primary PCI. They were subjected to full clinical examination, laboratory investigation including CRP and serum

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albumin, 12 leads surface ECG, echocardiography and primary percutaneous coronary intervention (PCI).

Results: There was significant statistical difference between both groups as regard age (> 60 years, 96.7% vs 20%, $P < 0.001$), gender (male, 93.3% vs 63.3%, $P = 0.002$), ischemia time (> 6 hours, 100% vs 33.3%, $P < 0.001$), CRP level (64 ± 32.6 mg/L vs 26.27 ± 21.5 mg/L, $P < 0.001$), serum albumin (3.22 ± 0.23 g/dL vs 3.55 ± 0.20 g/dL, $P < 0.001$), CRP albumin ratio (CAR) (0.0204 ± 0.011 vs 0.0076 ± 0.0064, $P < 0.001$), coronary artery ectasia (30% vs 6.7%, $P = 0.003$), thrombus grade score (≥ 4, 100% vs 10%, $P < 0.001$). However, there was no significant statistical difference between both groups as regard smoking, dyslipidemia and revascularization method.

Conclusion: Compared to CAE, CAR is more significant and more reliable to predict no reflow in acute STEMI patients managed by primary PCI within 24 hours of presentation.

Keywords: No reflow; percutaneous coronary intervention; coronary artery ectasia; CRP albumin ratio.

1. INTRODUCTION

Timely reperfusion of the infarct-related coronary artery using percutaneous coronary intervention (PCI) is the optimum ST segment elevation myocardial infarction (STEMI) treatment, reducing infarct size, minimizing myocardial damage, preserving ventricular function, and decreasing morbidity and mortality. Yet, despite opening the affected epicardial coronary artery, myocardial perfusion may sometimes not be restored, even resulting in no-reflow [1,2].

The no-reflow phenomenon is a serious complication and an independent risk factor for worse clinical adverse outcome. No-reflow is a multifactorial and complex phenomenon that causes perfusion deficits in the microvasculature [3].

Coronary artery ectasia (CAE) is defined as an inappropriate dilation of the coronary arteries, exceeding the diameter of normal adjacent segments by 1.5 times. The prevalence of CAE has been estimated in several angiographic studies to range between 1.2% and 5.3%. Even though its pathogenesis remains elusive, more than half of CAE cases have been ascribed to coronary atherosclerosis [4].

Coronary artery ectasia is common in males and hypertension is a risk factor. However, it can be present congenitally associated with other cardiac abnormalities such as bicuspid aortic valve, aortic root dilatation, ventricular septal defect or pulmonary stenosis. Also it can be acquired with atherosclerosis (the most common etiology), Kawasaki disease, mycotic and infectious septic emboli including syphilis and borreliosis, connective tissue diseases and Marfan's syndrome, arteritis, e.g., polyarteritis nodosa, Takayasu's disease, systemic lupus erythematosus [5].

Coronary artery ectasia has been suggested to be associated with no-reflow. High thrombus load is an independent predictor for distal embolization, and has been also associated with no-reflow. In CAE there is often a high thrombus load, because of the high thrombotic potential caused by altered blood flow patterns in the dilated coronary and local extensive inflammation [2].

The effect of inflammation on atherosclerosis development and destabilization has been more clearly understood in recent years, and inflammatory biomarkers are now increasingly being used in coronary artery disease (CAD) screening and prognosis [6].

C-reactive protein (CRP), one of the most commonly used biomarkers for this purpose, has been associated with increased development of myocardial infarction and stroke in healthy subjects, severity of CAD, recurrent coronary events, and mortality in patients with stable CAD and acute coronary syndromes. During the start of the illness, the degree of inflammation is linked to the level of CRP [6].

Albumin is the major protein in human plasma and the most abundant circulating protein in the extracellular compartment. Albumin has multiple important physiological functions including maintenance of plasma osmotic pressure and capillary permeability, it is a ligand for many endogenous and exogenous compounds and

affects pharmacokinetics of many drugs [7]. It is a negative acute-phase protein, so the level of hypo-albuminaemia in patients that are critically ill is linked to the intensity of the infection triggered inflammatory response [6].

No-reflow in STEMI patients has been linked to the CRP and albumin levels. For this reason, using the two parameters in combination, i.e. the CRP to albumin ratio, where the higher ratio indicates inflammation, could have a better chance of predicting no-reflow than if they work individually [6].

2. PATIENTS AND METHODS

2.1 Patients

This study was conducted on 90 patients admitted with acute STEMI and treated with primary PCI within 24 hours of presentation at cardiovascular medicine department Tanta university hospitals. This is a prospective study and data collection was done within 12 months started from June 2018. Patients were divided into 2 groups:

2.1.1 Group 1 (Case group)

Patients with no-reflow phenomenon, patients with thrombolysis in myocardial infarction (TIMI) 0-1 flow post primary PCI, in the absence of dissection, thrombus, spasm or high-grade residual stenosis, were considered as no-reflow case.

2.1.2 Group 2 (Control group)

Two consecutive STEMI patients after each case, with TIMI flow ≥ 2 after primary PCI.

Exclusion criteria: Patients with acute coronary syndrome other than STEMI, coronary artery dissection, coronary artery spasm, high-grade residual coronary stenosis, previous myocardial infarction, previous PCI and previous CABG were all excluded.

2.2 Methods

All included patients were subjected to full history taking including risk factors for coronary artery ectasia, full clinical examination including general and local cardiac examination, 12 lead electrocardiogram (ECG), echocardiography (using a GE vivid seven cardiac ultrasound phased array system with tissue doppler imaging using M4S transducer 4 M.HZ.), primary PCI (no-reflow was based on TIMI flow post-PCI, we did not include the myocardial blush grade (MBG) score because this was not always scored properly) and routine laboratory investigations including complete blood count, random blood sugar, renal function tests and CRP/Albumin ratio (CAR). The usual CRP level ranged from 0–19 mg/L, the albumin level ranged from 3.5–5.5 g/dL. The CAR is derived by dividing the CRP with the albumin level and multiplying it by 10.

2.3 Statistical Analysis

Statistical analysis of the present study was calculated by SPSS software package version 25.The qualitative parameters were described by number of frequency and percentage while the quantitative variables were described by mean, standard deviation and range. Normality of qualitative variables was tested by Kolmogorov-Smirno test. The comparison of independent quantitative variables was calculated by T independent test. The comparison between two qualitative variables was done by Chi square, Fisher's exact fisher and Monte Carlo tests. The risk estimate was evaluated by odds ratio with 95% confidence interval.

3. RESULTS

There were 30 cases and 60 controls. The present study compares between the two groups regarding demographic data, risk factors, family history, past cardiac history, clinical presentation, angiographic findings, laboratory results, LV systolic function and outcomes during hospitalization.

3.1 Regarding Demographic Data, Prevalence of Risk Factors and Clinical Characteristics

In the no reflow group of our study as shown in Table 1, male patients represented the majority of the no reflow cases (93.3% vs 63.3%, P = 0.002) compared to the control group. Patients in the no reflow group were found aged > 60 years (96.7% vs 20%, P < 0.001) and they had a significantly higher prevalence of diabetes mellitus (83.3% vs 53.3%, P = 0.005) and hypertension (86.7% vs 50%, P < 0.001). The admission systolic blood pressure of the patients in the no reflow group was < 90 mmHg (66.7% vs 10%, P < 0.001) with admission random blood glucose of > 300 mg/dl (83.3% vs 33.3%, P <

0.001). Patients of the no reflow group presented mainly with anterior STEMI (73.3% vs 26.7%, *P* < 0.001), Killip class ≥ 3 (66.7% vs 10%, *P* < 0.001) and with ischemia time > 6 hours (100% vs 33.3%, *P* < 0.001).

Between the two groups, there were no statistically significant differences regarding smoking, dyslipidemia, family history of coronary artery diseases and heart rate.

3.2 Regarding Angiographic and Procedural Characteristics

In the no reflow group of the current study as shown in Table 2, LAD was predominantly the IRA (76.7% vs 46.7%, *P* = 0.007) compared to the control group. Also in the no reflow group, the IRA lesion was predominantly proximal (73.3% vs 26.7%, *P* < 0.001) with longer lesion length > 20 mm (100% vs 20%, *P* < 0.001).

Additionally, multi-vessel disease was more often found in the no reflow group (40% vs 6.7%, *P* < 0.001). Regarding thrombus burden, thrombus grade score was ≥ 4 in all patients of the no reflow group (100% vs 10%, *P* < 0.001). In the case group, ectatic IRA was present in 9 patients (30%) while in the control group, it was found only in 4 patients (6.7%) (*P* = 0.003).

There was no significant difference regarding pre-procedural TIMI flow score between the two groups. TIMI flow 0-1 pre-PCI was found in all patients of no reflow group (100% vs 91.7%, *P* = 0.162). Also, there was no significant difference regarding revascularization method between the two groups.

Table 1. Demographic data, prevalence of risk factors and clinical characteristics in both groups

		No reflow n = 30	Control n = 60	OR	X^2	P Value
		No.	No.	95% C.I.		
Age	**> 60**	29 (96.7%)	12 (20%)	116	47.3	< 0.001
	< 60	1 (3.3%)	48 (80%)	14.33 - 939.19		
Gender	**Male**	28 (93.3%)	38 (63.3%)	8.105 (if male)	9.205	0.002
	Female	2 (6.7%)	22 (36.7%)	1.76 - 37.34		
Diabetes mellitus		25 (83.3%)	32 (53.3%)	4.375	7.751	0.005
				1.48 - 12.96		
Systemic Hypertension		26 (86.7%)	30 (50%)	6.5	11.439	< 0.001
				2.02 - 20.9		
Smoking		14 (46.7%)	36 (60%)	0.583	1.44	0.23
Dyslipidemia		14 (46.7%)	28 (46.7%)	1	0	1
Family History PCAD		9 (30%)	10 (16.7%)	2.143	2.135	0.144
SBP	**< 90 mmHg**	20 (66.7%)	6 (10%)	18	31.26	< 0.001
	> 90 mmHg	10 (33.3%)	54 (90%)	5.79 - 55.99		
Heart rate	**> 75 b/min**	23 (76.7%)	50 (83.3%)	1.522	0.58	0.446
	< 75 b/min	7 (23.3%)	10 (16.7%)			
RBG	**> 300 mg/dl**	25 (83.3%)	20 (33.3%)	10	20	< 0.001
	< 300 mg/dl	5 (16.7%)	40 (66.7%)	3.33 - 30.4		
Killip III or IV		20 (66.7%)	6 (10%)	18	31.262	< 0.001
				5.79 - 55.99		
Infarction localization					28.31	<0.001
	Anterior	22 (73.3%)	16 (26.7%)	7.56	17.8	<0.001
				2.81 - 20.37		
	Inferior	8 (26.7%)	10 (16.7%)	1.8	1.25	0.264
				0.6 - 5.2		
	Lateral	0 (0%)	28 (46.7%)		20.3	<0.001
	Others	0 (0%)	6 (10%)			
Ischemic Time	**> 6 hours**	30 (100%)	20 (33.3%)		36	< 0.001
	< 6 hours	0 (0%)	40 (66.7%)			

OR: odd ratio, X^2: Chi square test, CI: confidence interval, PCAD: previous coronary artery disease, SBP: systolic blood pressure, RBG: random blood glucose

CAE was found in 13 patients (14.44%) of the whole study population. Baseline and angiographic characteristics of patients with or without CAE of the IRA were summarized in Table 3.

Compared to non-ectatic IRA patients, the ectatic IRA patients were males (100% vs 68.8%, *P* = 0.02), aged > 60 years (76.9% vs 40.3%, *P* = 0.01), hypertensive (100% vs 55.8%, *P* = 0.002) and smokers (84.6% vs 50.6%, *P* = 0.02). They showed higher frequency of inferior STEMI (76.9% vs 10.4%, *P* < 0.001) and a lower frequency of anterior and lateral STEMI (15.4%, 7.7% vs 46.8%, 35.1% respectively, *P* < 0.001).

The IRA was predominantly the RCA (61.5% vs 11.7%, *P* < 0.001) and the lesion is predominantly mid-segment (69.2% vs 32.5%, *P* = 0.011). Longer lesion length (76.9% vs 41.6%, *P* = 0.02) and higher thrombus burden (100% vs 29.9%, *P* < 0.001) were significantly more often present in patients with CAE. Patients with CAE had a significantly higher prevalence of no-reflow (69.2% vs 27.3%, *P* = 0.003).

3.3 Regarding Laboratory Findings

As shown in Table 4, the mean admission total leukocyte count (13.36 ± 1.14 x 10^9 cells/L vs 11.68 ± 1.28 x 10^9 cells/L, *P* < 0.001), mean serum creatinine (1.44± 0.26 mg/dl vs 1.16 ± 0.23 mg/dl, *P* < 0.001) and mean CRP level (64 ± 32.6 mg/L vs 6.27 ± 21.5 mg/L, *P* < 0.001) were significantly higher in the no-reflow group while mean serum albumin (3226.6 ± 237.7 mg/L vs 3546.6 ± 201.2 mg/L, *P* < 0.001) was significantly lower in the no-reflow group. There was no statistical difference between both groups regarding hemoglobin concentration.

Table 2. Angiographic and procedural characteristics in both groups

	No reflow n = 30	Control n = 60	OR	X^2	P Value
	No.	No.	95% C.I.		
Infarcted related artery				9.112	0.01
LAD	23 (76.7%)	28 (46.7%)	3.76 1.4 - 10.07	7.33	0.007
LCX	2 (6.7%)	20 (33.3%)	0.14 0.03-0.6	7.7	0.006
RCA	5 (16.7%)	12 (20%)	0.8 0.25-2.5	0.14	0.703
Lesion localization				20.786	<0.001
Proximal	22 (73.3%)	16 (26.7%)	7.5 2.8 - 20.3	17.8	<0.001
Mid	8 (26.7%)	26 (43.3%)		2.36	0.124
Distal	0 (0%)	18 (30%)		11.25	0.001
Multivessel disease	12 (40%)	4 (6.7%)	9.333	15.203	<0.001
Pre-procedural TIMI flow score					
1 or 0	30 (100%)	55 (91.7%)		2.647	0.162
2 or 3	0	5 (8.3%)			
Lesion length **< 20 mm**	0 (0%)	48 (80%)		51.429	< 0.001
> 20 mm	30 (100%)	12 (20%)			
Thrombus grade					
< 4	0 (0%)	54 (90%)		67.5	< 0.001
≥ 4	30 (100%)	6 (10%)			
Revascularization method					
PTCA	0 (0%)	6 (10%)		4.19	0.122
BMS	5 (16.7%)	14 (23.3%)			
DES	25 (83.3%)	40 (66.7%)			
Coronary artery ectasia	9 (30%)	4 (6.7%)	6 1.67 - 21.58	8.8	0.003

OR: odd ratio, X^2: Chi square test, CI: confidence interval, LAD: left anterior descending, LCX: left circumflex, RCA: right coronary artery, TIMI: thrombolysis in myocardial infarction, PTCA: percutaneous transluminal angioplasty, BMS: bare metal stent, DES: drug-eluting stent

Table 3. Baseline and angiographic characteristics of both ectatic and non ectatic infarct related artery groups

		Ectatic IRA n = 13	Non-ectatic IRA n = 77	X^2	P Value
		No.	No.		
Gender	**Male**	13 (100%)	53 (68.8%)	5.53	0.02
	Female	0 (0%)	24 (31.2%)		
Age	**> 60**	10 (76.9%)	31 (40.3%)	6.03	0.01
	< 60	3 (23.1%)	46 (59.7%)		
Diabetes mellitus		11 (84.6%)	46 (59.7%)	2.96	0.09
Systemic Hypertension		13 (100%)	43 (55.8%)	9.23	0.002
Smoking		11 (84.6%)	39 (50.6%)	5.2	0.02
Dyslipidemia		6 (46.2%)	36 (46.8%)	0.002	0.97
Family History of PCAD		4 (30.8%)	15 (19.5%)	0.85	0.36
Lesion length					
	< 20 mm	3 (23.1%)	45 (58.4%)	5.59	0.02
	> 20 mm	10 (76.9%)	32 (41.6%)		
Lesion localization				7.49	0.02
	Proximal	4 (30.8%)	34 (44.2%)	0.81	0.366
	Mid	9 (69.2%)	25 (32.5%)	6.39	0.011
	Distal	0 (0%)	18 (23.4%)	3.79	0.051
Infarcted related artery				19.21	<0.001
	LAD	2 (15.4%)	49 (63.6%)	10.5	0.001
	LCX	3 (23.1%)	19 (24.7%)	0.015	0.901
	RCA	8 (61.5%)	9 (11.7%)	18	<0.001
Pre-procedural TIMI flow score					
	< *2*	11 (84.6%)	74 (96.1%)	2.79	0.15
	≥ 2	2 (15.4%)	3 (3.9%)		
Revascularization method					
	PTCA	4 (30.8%)	2 (2.6%)	14.78	0.003
	BMS	1 (7.7%)	18 (23.4%)		
	DES	8 (61.5%)	57 (74%)		
Thrombus grade	**< 4**	0 (0%)	54 (70.1%)	22.79	<0.001
	≥ 4	13 (100%)	23 (29.9%)		
Myocardial infarction localization				30.9	<0.001
	Anterior	2 (15.4%)	36 (46.8%)	4.48	0.034
	Inferior	10 (76.9%)	8 (10.4%)	30.7	<0.001
	Lateral	1 (7.7%)	27 (35.1%)	3.88	0.049
	Others	0 (0%)	6 (7.8%)		
No Reflow (TIMI 0 - 1)		9 (69.2%)	21 (27.3%)	8.8	0.003

IRA: infarcted related artery, X^2: Chi square test, PCAD: previous coronary artery disease, TIMI: Thrombolysis in Myocardial Infarction, PTCA: percutaneous transluminal coronary angioplasty, BMS: bare-metal stent, DES: drug eluting stent, LAD: left anterior descending, LCX: left circumflex coronary, RCA: right coronary artery

Consequently by dividing the CRP with the serum albumin level in mg/L to get the CAR, mean CAR was higher in the no reflow group (0.0204 ± 0.011 vs 0.0076 ± 0.0064, $P < 0.001$).

3.4 Regarding the Left Ventricular Ejection Fraction

Left ventricular ejection fraction (LVEF) was significantly lower in the no-reflow group before primary PCI compared to the control group (LVEF < 40%, 76.7% vs 30%, $P < 0.001$).

3.5 Regarding Short Term Complications

In the current study, 20 patients of the no reflow group had experienced cardiogenic shock during their hospital stay (66.7% vs 13.3%, $P < 0.001$) compared to the control group. Regarding in-hospital mortality, 27 patients of the study population died during their hospital stay. In the no reflow group, 21 patients (70% vs 10%, $P < 0.001$) died during hospital stay compared to the control group.

There was no significant difference regarding malignant arrhythmias experience between the two groups (Table 5).

3.6 ROC curve for CRP/Albumin Ratio to Predict no Reflow

The receiver operating characteristic (ROC) analysis showing the performance and predictive accuracy of CAR in predicting no reflow, the area under the curve (AUC) was 0.843, confidence interval (CI) 0.752 – 0.933 (P < 0.001),with cutoff value CAR more than > 0.0103, with 80 % sensitivity and 80% specificity (Fig. 1) (Table 6)

In group I: CAR was ≥ 0.0103 in 24 patients (80%) and < 0.0103 in 6 patients (20%) while **in group II***:* CAR was ≥ 0.0103 in 12 patients (20%) and < 0.0103 in 48 patients (80%).

So it is statistically highly significant for predicting no reflow (≥ 0.0103, OR 16, 95% C.I 5.35 – 47.86, *P* < 0.001) (Table 7).

Table 4. Laboratory findings difference between the no reflow and the control groups

	No reflow n = 30	Control n = 60	T	P Value
	Mean ± SD (Range)	Mean ± SD (Range)		
Hemoglobin concentration (g/dL)	12.53 ± 0.54 (11.2 – 13.5)	12.46 ± 0.73 (11.1 – 13.6)	0.442	0.659
Total leukocyte count (1000 cells/ cu mm)	13.36 ± 1.14 (11.3 – 15.2)	11.68 ± 1.28 (9.7 – 14.7)	6.291	< 0.001
Serum Creatinine (mg/dL)	1.44± 0.26	1.16 ± 0.23	4.991	< 0.001
C-reactive protein (mg/L)	(0.9 – 1.9)	(0.7 – 1.6)		
Albumin (mg/L)	64 ± 32.6 (12 – 96)	26.27 ± 21.5 (6 – 112)	6.56	< 0.001
C-reactive protein /Albumin ratio	3226.6 ± 237.7 (2800 – 3700)	3546.6 ± 201.2 (3100 – 4000)	-6.326	< 0.001
	0.0204 ± 0.011 (0.0032 – 0.0343)	0.0076 ± 0.0064 (0.0016 – 0.0329)	6.9	< 0.001

T: independent t-test, SD: standard deviation

Table 5. Left ventricular ejection fraction and common short term complications in both groups

	No reflow n = 30	Control n = 60	OR	X^2	P Value
	No.	No.	95% C.I		
LVEF < 40 %	23 (76.7%)	18 (30%)	7.66 2.79 – 21.05	17.56	< 0.001
Malignant arrhythmia	2 (6.7%)	4 (6.7%)	1	0	1
Cardiogenic shock	20 (66.7%)	8 (13.3%)	13	26.544	< 0.001
In Hospital Mortality	21 (70%)	6 (10%)	21	34.286	< 0.001

OR: odd ratio, X^2: Chi square test, CI: confidence interval, LVEF: left ventricular ejection fraction

Table 6. Analysis of ROC for CAR

Positive if CAR ≥	Sensitivity	Specificity
0.006958	83%	57%
0.007165	83%	77%
0.0103	80%	80%
AUC	0.843	
	P value < 0.001	
	Lower 0.752	
	Upper 0.933	

AUC: area under the curve, CAR: C-reactive protein albumin ratio

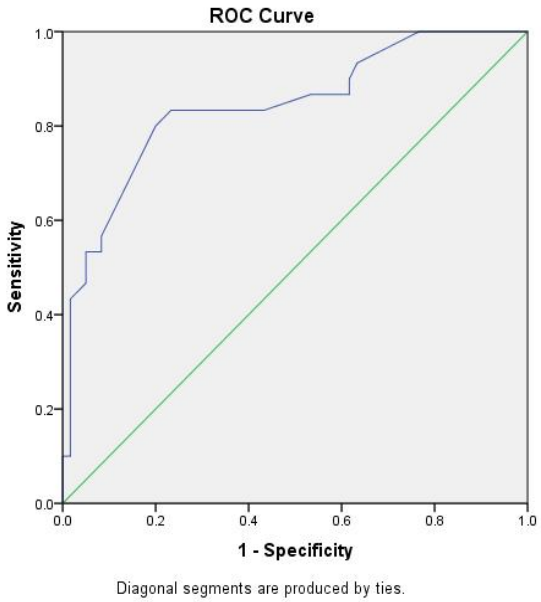

Fig. 1. ROC curve for CAR to predict no reflow

Table 7. CAR in no reflow and control groups

	No reflow (n=30)	Control (n=60)	OR	X^2	P Value
	No.	No.	95% C.I.		
CAR ≥ 0.0103	24 (80%)	12 (20%)	16 5.35 - 47.86	30	<0.001

OR: odd ratio, X^2: Chi square test, CI: confidence interval, CAR: C-reactive protein albumin ratio

4. DISCUSSION

Although primary PCI is the most advantageous and rewarding reperfusion strategy available in patients with acute STEMI, it fails to restore optimal myocardial reperfusion in a sizeable portion of patients, mostly because of no-reflow phenomenon [8].

According to Kloner et al. [9] no reflow is defined as suboptimal myocardial reperfusion through a part of coronary circulation without angiographic evidence of mechanical vessel obstruction. The term ‘‘no-reflow’’ should be reserved for patients with thrombolysis in myocardial infarction (TIMI) grade 0 or 1 flow in the absence of other etiologies with ‘‘slow flow’’ referring to TIMI grade 2 flow.

Several recent studies have investigated clinical and procedural predictors of no reflow in patients with STEMI treated with primary PCI. In this study we are focusing on the C-reactive protein/albumin ratio and the coronary artery ectasia as independent predictors of no reflow.

No-reflow in STEMI patients has been linked to the CRP and albumin levels. For this reason, using the two parameters in combination, i.e. the CRP to albumin ratio, where the higher ratio indicates inflammation, could have a better chance of predicting no-reflow than if they work individually [6].

Also, Coronary artery ectasia has been suggested to be associated with no-reflow. High thrombus load is an independent predictor for distal embolization, and has been also associated with no-reflow. In CAE there is often a high thrombus load, because of the high thrombotic potential caused by altered blood flow patterns in the dilated coronary and local extensive inflammation [2].

To the best of our knowledge, this is the first study to assess and compare the significance of CRP/albumin ratio versus coronary artery ectasia

as predictors of the adverse no-reflow phenomenon in patients of acute STEMI undergoing primary PCI.

This is a prospective study was conducted on 90 patients admitted with acute STEMI at cardiovascular medicine department Tanta university hospitals. Data collection was done within 12 months started from June 2018. The pre-intervention routine blood sampling including CRP & albumin were examined in all patients, and they all underwent primary PCI within 24 hours of presentation.

Patients were divided into 2 groups according to the post primary PCI thrombolysis in myocardial infarction (TIMI) flow score into:

Group I: (Case group) 30 patients with no-reflow phenomenon, patients with TIMI 0-1 flow post primary PCI, in the absence of dissection, thrombus, spasm or high-grade residual stenosis, were considered as no-reflow case.

Group II: (Control group) 60 patients with TIMI flow ≥ 2 after primary PCI.

4.1 Regarding CRP Level in Both Groups

There was statistically significant difference between the two groups, as we found that CRP level ranged from 12 – 96 mg/L with mean 64 ± 32.6 mg/L in the case group, while in the control group, CRP level ranged from 6 – 112 mg/L with mean 26.27 ± 21.5 mg/L. (P < 0.001)

This came in agreement with the study conducted by Gjin Ndrepepa et al. [8] that included 1140 patients with ST-segment elevation myocardial infarction undergoing primary PCI, showing an independent association between baseline C-reactive protein level and no reflow, this study suggests that baseline inflammation may increase the risk of no reflow after primary PCI. One mechanism by which higher levels of C-reactive protein promote development of no reflow may involve suggestion that elevated level of C-reactive protein may increase infarct size by activating the complement cascade in the ischemic/necrotic tissue. Additionally, elevated level of C-reactive protein or other inflammatory molecules may promote microvascular obstruction through an array of mechanisms. However, the association between baseline inflammation and development of no reflow remains controversial [8].

Also, our study came in agreement with the study of Min Liu et al. [10], a study conducted over 136 STEMI patients with single coronary artery disease undergoing primary PCI to explore high-sensitivity C-reactive protein (hs-CRP) and endothelin-1 (ET-1) expressions in patients with no-reflow phenomenon. This study concluded that hsCRP and ET-1 levels significantly increased in patients with no-reflow phenomenon [10].

Similarly, our study agreed with the study of Alparslan Kurtul et al. [11] that found that hs-CRP was significantly higher in the no reflow cases and thus, an independent predictors of angiographic no-reflow (P < .001).

4.2 Regarding Serum Albumin (SA) Level

There was statistically significant difference between the two groups of our study, as we found that serum albumin level ranged from 2800 – 3700 mg/L (2.8 - 3.7 g/dL) in the case group with mean 3226.6 ± 237.7 mg/L, while in the control group, serum albumin level ranged from 3100 – 4000 mg/L (3.1 - 4 g/dL) with mean 3546.6 ± 201.2 mg/L. (*P* < 0.001)

This agrees with the study conducted by Alparslan Kurtul et al. [11] where a total of 536 STEMI patients who underwent PPCI were enrolled to investigate the association between baseline SA levels and no-reflow. This study demonstrated that decreased pre-procedural SA levels display a significantly and strongly independent association with no-reflow phenomenon.

Also, this agreed with a study conducted by Yavuz Karabağ et al. [6] where the albumin level was significantly lower in the no-reflow group than in the normal flow group (P < 0.001).

4.3 Regarding CRP/Albumin Ratio (CAR)

Hence, by evaluating the CRP/albumin ratio that could have a better chance of predicting no-reflow than if they work individually, we found accordingly that there was statistically significant difference between the two groups. In group I, CAR ranged from 0.0032 – 0.0343 with mean 0.0204 ± 0.011, while in group II, CAR ranged from 0.0016 – 0.0329 with mean 0.0076 ± 0.0064 (P < 0.001).

This came in concordance with the study conducted by Yavuz Karabağ et al. [6] where a total of 1217 consecutive STEMI patients who achieved epicardial vessel patency with PPCI

were recruited. This study showed that the increase in CAR is associated with imperfect reperfusion and is an independent predictor of angiographic no reflow development.

Also, Alparslan Kurtul et al. [11] study showed that lower SA levels are associated with increased inflammatory burden in the body as inflammation has been associated with decreasing albumin synthesis rate and increasing catabolism. And so, baseline serum albumin levels together with hs-CRP levels were significantly higher in patients with a no-reflow phenomenon, indicating the effect of inflammation in no-reflow pathogenesis as had been suggested by previous findings.

4.4 Regarding Presence of Coronary Artery Ectasia (CAE) at the Infarcted Related Artery (IRA)

In our study, ectatic IRA was found in only 13 patients (14.44%) of the whole limited study population sample size. However, there was statistically significant difference between the two groups. We found that in the case group, ectatic IRA is present in 9 patients (30%) while in the control group, it was found only in 4 patients (6.7%) (*P* = 0.003), rendering CAE significant and independent predictor to no reflow.

The prevalence of CAE in the general population varies. In an autopsy study the prevalence of CAE was 1.4%. For patients referred for a diagnostic coronary angiography the prevalence varied between 0.1 - 2.7%. When patients underwent a coronary angiography because of an acute coronary syndrome the prevalence of CAE was between 2.6-4.9% [2].

This low prevalence of CAE resulted in very few cases of ectatic IRA. Therefore in this study, the available data on the influence of CAE on angiographic outcome in STEMI patients are quite limited and making the study of the risk factors, demographic and clinical characteristics for the cases of CAE quite difficult.

However in the current study, patients with CAE had a significantly higher prevalence of no-reflow (69.2% vs 27.3%, P = 0.003). Somehow, our results came in agreement with the case-control study conducted by H.C.F. Schram et al. [2] that aimed at determining the potential association between CAE and no-reflow after primary PCI. A total of 231 STEMI patients underwent primary PCI. They were divided into 77 cases (no reflow) and 154 controls (normal flow).

Interestingly in their study, ectatic IRA was found also in only 32 patients (13.85%) of the whole study population. In CAE there is often a high thrombus load, because of the high thrombotic potential caused by altered blood flow patterns in the dilated coronary and local extensive inflammation. Therefore, similarly, the frequency of CAE was significantly higher (33.8% vs 3.9%, p < 0.001) in the no-reflow group compared to the control group [2].

Consequently, their study concluded that CAE is a strong and independent predictor of no-reflow after primary PCI for STEMI [2].

Also, in a study conducted by Gokturk Ipek et al. [12] that aimed to assess the risk factors and outcomes in STEMI patients with ectatic IRA who underwent PPCI, it was found that no-reflow rates were significantly higher (13.1% vs 5.4%, P = 0.004) in the CAE group compared to the non-ectatic group.

The receiver operating characteristic (ROC) analysis showed the performance and predictive accuracy of CAR in predicting no reflow in our study, the area under the curve (AUC) was 0.843, confidence interval (CI) 0.752 – 0.933 (P < 0.001),with cutoff value CAR more than > 0.0103, with 80 % sensitivity and 80 % specificity. Accordingly, CAR was ≥ 0.0103 in 80% of the patients of the no reflow group and was < 0.0103 in 80% of the control group patients.

In the study by Yavuz Karabağ et al. [6], a CAR cut-off value of 0.059 was selected for predicting angiographic NR with a sensitivity of 54.7% and specificity of 86.7%.

However, CAE significance as a predictor to no reflow might have been relatively underestimated in this study. As we mentioned before, this could be due to the low prevalence of CAE in general population so that in this limited sample size we got very few cases of ectatic IRA. Thus, it is quite possible that with a larger sample size, we could have studied more easily the prevalence of risk factors, demographic and clinical characteristics related to the CAE cases and the more precise influence of CAE on angiographic outcome in STEMI patients after PPCI.

5. CONCLUSION

According to the previously stated findings in our study regarding CAR and CAE and their association to the no reflow phenomenon, we found that C-reactive protein albumin ratio is more significant and more reliable with cutoff value CAR > 0.0103, with 80 % sensitivity and 80 % specificity to predict no reflow in acute STEMI patients managed by primary PCI within 24 hours of presentation compared to coronary artery ectasia.

STUDY LIMITATIONS

The present study has several limitations. First, this is a single-center experience in only 12 months of duration representing a small size of study population. Also, the prevalence of CAE in the general population is very low. This low prevalence of CAE resulted in very few cases of ectatic IRA. Therefore in this study, the available data on the influence of CAE on angiographic outcome in STEMI patients are quite limited and making the study of the risk factors, demographic and clinical characteristics for the cases of CAE quite difficult. However, the study population included homogenous patients with STEMI undergoing primary PCI within 24 hours from symptom onset in certain months, thus mirroring the real world scenario.

Second, our definition of no-reflow was based on TIMI flow post-PCI. We did not include the myocardial blush grade (MBG) score in our definition, because this was not always scored properly. This could have led to selection of only the worst no-reflow cases.

Third, intravascular ultrasound (IVUS) hasn't been used to quantitatively evaluate thrombus burden and plaque content. However, IVUS can prolong a PCI procedure and is more expensive than conventional primary PCI. Moreover, non-invasive measures as myocardial contrast echocardiography (MCE) and contrast-enhanced cardiovascular magnetic resonance (CEMR) which can detect no-reflow and also define the extent of myocardium affected didn't be used.

Fourth, the low use of thrombus-aspirating device, which may improve myocardial reperfusion, but we did not routinely perform thrombus aspiration in our study.

Lastly, other cause of elevated CRP and hypo-albuminaemia were very difficult to be carefully excluded in our study population. Also, it is recommended for further research and use of hs-CRP to get more accurate data results.

CONSENT

An informed and written consent was taken from all participants.

ETHICAL APPROVAL

As per international standard written ethical permission has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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