



## ASSOCIATION BETWEEN REPERFUSION TIME, CTFC AND INFLAMMATORY BIOMARKERS IN STEMI PATIENTS

Morteza Safi<sup>1</sup>, Reza Arian Nia<sup>2</sup>, Mohammad Hasan Namazi<sup>3</sup>, Habibollah Saadat<sup>4</sup>, Hossein Vakili<sup>5</sup>, Saeed Alipour Parsa<sup>6</sup>, Isa Khareshi<sup>7</sup>

1,7. Cardiovascular Research Center, Modarres hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

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### ABSTRACT

We investigated inflammatory markers such as erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), CTFC and time to intervention in myocardial infarction with persistent ST-segment elevation (STEMI) undergoing primary angioplasty.

**Material and Method:** A cohort of 104 consecutive patients with STEMI undergoing primary PCI was enrolled. Relationship between patients ESR and CRP at the time of admission and CTFC and pain duration was evaluated.

**Results:** Our data showed that the higher ESR and CRP the more CTFC. In our study there no correlation was detected between CTFC and ESR and CRP after intervention (p= no significant). In our study mean±SD for CTFC measures according to pain duration before PPCI (less than 2 compared with more than 6 hours) were defined as 20.17±2.22 and 31.84±5.84, respectively. Increasing time before reperfusion was associated with higher CTFC values (p=0.001).

**Conclusion:** Elevated ESR and CRP at the time of admission are associated with higher CTFC values in STEMI patients treated with reperfusion therapy. Lower time to reperfusion has important role in reducing ESR and CRP at the time of admission and CTFC values that can improve patients' survival with AMI undergoing PPCI.

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### Introduction

Nowadays coronary artery disease is the most important and leading cause of death in almost all communities. One of the most imperative of CAD manifestations is myocardial infarction (MI) which can be detected by cardiologist as first manifestation [1, 2]. MI is a clinical status that almost begins with chest pain and releasing biomarkers of Myocytes. It can be accompanied by ST segment elevation which is called STEMI and sometimes without elevation in ST segment which is called NSTEMI. STEMI prevalence has been declined over the past years whereas NSTEMI's prevalence has begun to rise [3]. Recognition of myocardial infarction (MI) is by clinical manifestations such as electrocardiographic findings, alteration in values of myocardial cells specific biomarkers which release in plasma after necrosis and different imaging methods [4]. First time PCI was used for single vessel coronary disease in 1977 but with the advances in operators' skills and equipment's technology we are able to use it for multi-vessel diseases [5]. In newest AHA guideline, it recommends for implementation of primary PCI only for culprit coronary artery and PCI for non-infarcted artery its recommended to do PCI if the patient is hemodynamically stable [6].

The thrombolysis in myocardial infarction (TIMI) flow grading system is a qualitative process for assessing reperfusion strategy. On the other hand, the corrected TIMI frame count (CTFC) is a quantitative method to evaluate the TIMI flow grading

system. Recently, CTFC has been proposed as a simple, inexpensive, reproducible and quantitative method to measure coronary blood flow [7, 8]. We investigated inflammatory markers such as erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), CTFC and time to intervention in myocardial infarction with persistent ST-segment elevation (STEMI) undergoing primary angioplasty.

### Materials and Methods

This cohort study was conducted on patients who had received Primary PCI with diagnosis of STEMI. After sterile preparation and injection of 2% lidocaine at the puncture site, an arterial sheath was used to enter the femoral artery. Overall, 104 patients, including 88 (84.6%) men and 16 (15.4%) women, were included. STEMI was defined as typical chest pain and the presence of electrocardiographic criteria. Written, informed consent was obtained from each patient.

After history taking and physical examination on admission, door- to-balloon time, systolic blood pressure, location of myocardial infarction (MI), CTFC and in-hospital adverse events was filled out for all patients. Door-to-balloon time was defined as the interval between arrival to the hospital and the use of a therapeutic device (thrombectomy catheter, balloon, and stent). Inflammatory markers such as erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), CTFC and time to intervention in patients with ST-segment elevation (STEMI) undergoing primary angioplasty were evaluated.

Statistical analyses

Data are shown as means  $\pm$  SD. Chi-square test was used for categorical variables and independent Student's t-tests or ANOVA tests for continuous variables. Categorical variables were contrasted by the chi-square test (or Fisher's exact test as needed). Statistical analyses were performed with SPSS software for Windows (Statistical Product and Service Solutions, version 16.0, SSPS Inc, Chicago, IL, USA). A P value of 0.05 was considered significant.

### Results

Among 104 patients, 88 (84.6%) and 15 (15.4%) were men and women, respectively. Mean age was  $59.8 \pm 11.5$  with a range of 28 to 79 years. Other baseline characteristics are outlined in Table 1. Culprit lesion distribution according to angiographic findings was as followed: LAD left anterior descending in 55 patients (52.9%), left circumflex in 12 (11.5%), right coronary artery in 37 (35.6), respectively.

The mean CTFC frame was  $26.8 \pm 6.4$ . In our study correlation between times to perfusion was and CTFC, and inflammatory biomarkers before and after intervention was assessed. As shown in table 2, mean  $\pm$  SD for CTFC measures according to pain duration before PPCI (less than 2 compared with more than 6 hours) were defined as  $20.1 \pm 2.2$  and  $31.8 \pm 0.9$ , respectively which was statistically significant ( $P=0.02$ ). Increasing time before reperfusion was associated with higher CTFC values ( $p=0.02$ ).

In this study relationship between patients ESR and CRP at the time of admission and CTFC and pain duration was evaluated. As showed in table 2, ESR at the time of admission in patients with pain duration more than 6 hours was significantly higher than patients with pain duration less than 2 hours before PPCI ( $41.2 \pm 2.5$  and  $26.8 \pm 4.1$ , respectively and  $p=0.002$ ). There was also significant association between reperfusion time and CRP before PPCI. But we did not detect correlation between ESR and CRP after intervention.

Our data showed the higher ESR and CRP at the time of admission the more CTFC. In our study there no correlation was detected between CTFC and ESR and CRP after intervention ( $p=$  no significant).

### Discussion

In this study relationship between patients ESR at the time of admission and CTFC and pain duration was evaluated. Increasing time before reperfusion was associated with higher ESR at the time of admission and CTFC values. Our data were along with previous studies. Previous reports have also shown an association between CAD and ESR [9]. Natali et al. showed that ESR was an independent indicator of the presence of CAD and cardiac death in patients undergoing elective coronary angiography [10]. Erikssen et al. showed that ESR was a very strong independent short- and long-term predictor of cardiac mortality in a large group of apparently healthy men [11]. ESR is in part established by these inflammatory markers and therefore may be related to inflammatory activity in the atherosclerotic lesions.

It is reported that elevated ESR is particularly associated with sudden death and long-term mortality in patients treated with reperfusion therapy for STEMI.

The slow/no-reflow phenomenon is a remarkable complication following direct PCI for AMI. Previous studies have revealed that both short- and long-term out-comes are poor in those who have developed the no-reflow phenomenon following direct PCI [12]. A study demonstrated that the no-reflow phenomenon after primary PCI is a strong predictor of death early in the 5 years after the acute event in patients with AMI [13].

CTFC is an independent predictor of in-hospital mortality following STEMI. Gibson et al. reported that patients with acute coronary syndrome who died after PCI had a higher CTFC compared to those who survived [14].

Our results revealed that increasing time before reperfusion was associated with higher CTFC values. French et al. found a significant correlation between CTFC and three-week survival after MI. They concluded that  $CTFC \geq 40$  is a predictor of adverse outcomes including mortality, 30-day in-hospital major adverse cardiac events, reinfarction, congestive heart failure, and left ventricular remodeling [15].

It is assumed that reduced CTFC measures would result in major cardiac events and improve cardiac function in patients undergone PPCI in patients with AMI. Liu et al. newly reported that 80 mg atorvastatin loading followed by 40 mg atorvastatin therapy could diminish the inflammatory response and get better the ejection fraction in patients with STEMI.

### Conclusion

Inflammation is known to be an important risk factor for the development of atherosclerotic events. Elevated ESR and CRP at the time of admission are associated with higher CTFC values in STEMI patients treated with reperfusion therapy.

Lower time to reperfusion has main role in reducing ESR and CRP at the time of admission and CTFC values that can improve patients' survival with AMI undergoing PPCI.

### Reference:

1. Berry JD, Dyer A, Cai X, Garside DB, Ning H, Thomas A, et al. Lifetime risks of cardiovascular disease. *N Engl J Med.* 2012;366(4):321-9.
2. Thygesen K, Alpert JS, Jaffe AS, Simoons ML, Chaitman BR, White HD. Third universal definition of myocardial infarction. *Circulation.* 2012;126(16):2020-35.
3. O'Gara PT, Kushner FG, Ascheim DD, Casey DE, Chung MK, De Lemos JA, et al. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction. *Circulation.* 2013;61(4):362-425.
4. Mohr FW, Morice MC, Kappetein AP, Feldman TE, Stähle E, Colombo A, et al. Coronary artery bypass graft surgery versus percutaneous coronary intervention in patients with three-vessel disease and left main coronary disease: 5-year follow-up of the randomized, clinical SYNTAX trial. *The lancet.* 2013;381(9867):629-38.
5. Levine GN, Bates ER, Blankenship JC, Bailey SR, Bittl JA, Cercek B, et al. 2015 ACC/AHA/SCAI focused update on primary percutaneous coronary intervention for patients with ST-elevation myocardial infarction: an update of the 2011 ACCF/AHA/SCAI guideline for percutaneous coronary intervention and the 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction. *Circulation.* 2016;133(11):1135-47.
6. Gibson CM, Cannon CP, Daley WL, et al. TIMI frame count: a quantitative method of assessing coronary artery flow. *Circulation.* 1996;93(5):879-88.
7. Morishima I, Sone T, Okumura K, et al. Angiographic no-reflow phenomenon as a predictor of adverse long-term outcome in patients treated with percutaneous transluminal coronary angioplasty for first acute myocardial infarction. *J Am Coll Cardiol.* 2000;36(4):1202-9.
8. Vijayalakshmi K, Kunadian B, Whittaker VJ, Williams D, Wright RA, Sutton AG, et al. The impact of chronically diseased coronary arteries and stenting on the corrected TIMI frame count in elective coronary angiography and percutaneous coronary intervention procedures. *Catheter Cardiovasc Interv.* 2007;70(5):691-700.
9. Corrado E, Novo S. High sensitivity of C-reactive protein in primary prevention. *G Ital Cardiol (Rome).* 2007;8(6):327-34.
10. Natali A, L'Abbate A, Ferrannini E. Erythrocyte sedimentation rate, coronary atherosclerosis, and cardiac mortality. *Eur Heart J.* 2003;7(7):639-48.
11. Erikssen G, Liestol K, Bjornholt JV, Stormorken H, Thaulow E, Erikssen J. Erythrocyte sedimentation rate: a possible marker of atherosclerosis and a strong predictor of coronary heart disease mortality. *Eur Heart J.* 2000;19(19):1614-20.
12. Esteves Filho A, Garcia DP, Martinez Filho EE. The no reflow phenomenon in the coronary arteries. *Arq Bras Cardiol.* 1999;72(1):99-108.
13. Ndrepepa G, Tiroch K, Fusaro M, Keta D, Seyfarth M, Byrne RA, et al. 5-year prognostic value of no-reflow phenomenon after percutaneous coronary intervention in patients with acute myocardial infarction. *J Am Coll Cardiol.* 2010;55(21):2383-9.

14. Gibson CM, Murphy SA, Rizzo MJ, Ryan KA, Marble SJ, McCabe CH, et al. Relationship between TIMI frame count and clinical outcomes after thrombolytic administration. Thrombolysis in myocardial infarction (TIMI) study group. *Circulation*. 1999;99(15):1945-50.
15. French JK, Hyde TA, Straznicky IT, Andrews J, Lund M, Amos DJ, et al. Relationship between corrected TIMI frame counts at three weeks and late survival after myocardial infarction. *J Am Coll Cardiol*. 2000;35(6):1516-24.
16. Liu HL, Yang Y, Yang SL, et al. Administration of a loading dose of atorvastatin before percutaneous coronary intervention prevents inflammation and reduces myocardial injury in STEMI patients: a randomized clinical study. *Clin Ther*. 2013;35(3):261-72.

**Table 1.** The Basic Characteristics of patients

<b>Table 1. Baseline Characteristics</b>	<b>(n=104)</b>	
Age (years)	59.8 ± 11.5	
Sex (Male/female)	(88/16)	
Smoking (%)	52	(50%)
Diabetes (%)	25	(24%)
Hypertension (%)	56	(53.8%)
Family History of IHD (%)	18	(17.3%)
Obesity (%)	17	(16.3%)
Dyslipidemia (%)	14	(13.5%)
CTFC (frame)	26.8± 6.4	
Culprit lesions (%)		
LAD	55	(52.9%)
LCX	12	(11.5%)
RCA	37	(35.6%)

**Table 2.** The correlation between times to perfusion was and CTFC, and inflammatory biomarkers before and after intervention

		<b>Time to reperfusion (hour)</b>			<b>P value</b>
	<2	2-4	4-6	>6	
	(n=24)	(n=31)	(n=14)	(n=35)	

<b>CTFC</b>	20.1±2.2	25.7± 5.7	27.8±1.2	31.8±0.9	0.02
<b>ESR before</b>	26.8± 4.1	29.9±2.1	41.5±4.8	41.2±2.5	0.002
<b>intervention</b>					
<b>ESR after</b>	20.6±4.1	15.1±1.8	19.5± 5.3	21.1± 2.9	0.9
<b>intervention</b>					
<b>CRP before</b>					
<b>intervention</b>					
<b>+1</b>	5 (20.8%)	16 (51.6%)	7 (50%)	12 (34%)	0.001
<b>+2</b>	3(12.5%)	6(19.4%)	4(28.6%)	17(48.6%)	
<b>+3</b>	0(0)	1(3.2)	3(21.4%)	4(11.4%)	
<b>CRP after</b>					
<b>intervention</b>					
<b>Normal</b>	16 (66.7%)	18 (58.1%)	9 (64.3%)	22 (62.9%)	0.4
<b>positive</b>	8 (33.3%)	13 (41.9%)	5 (35.5%)	13 (37.1%)	