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The In-Hospital Prognostic Value of High Sensitivity C-Reactive Protein in STEMI Patients Treated by Thrombolysis Versus Primary Percutaneous Coronary Intervention

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ABSTRACT

Introduction: Coronary artery disease (CAD) is considered a major causative agent of mortality and morbidity. Many reports recommended the use of C-reactive protein (CRP) as an inflammatory marker for its high sensitivity that could help in prevention of CAD.

Objective: This work aimed to clarify the in-hospital prognostic value of high-sensitivity CRP (hs-CRP) in ST-elevation myocardial infarction (STEMI) cases who are treated by thrombolysis vs. primary percutaneous coronary intervention (PCI) and comparing the outcome of the treatment between the two groups.

Patients and methods: 48 STEMI cases were divided into two groups in this cross-section study: Patients in group A had Primary PCI, whereas those in group B received thrombolysis treatment. Patients were evaluated by history, examinations, investigations and coronary angiography.

Results: Most of patients had grade II mitral regurge (68.8%) with statistical insignificant differences between the study groups. Most of patients had wall motion abnormalities in anterior septum (43.8%) with statistical insignificant difference between groups. In this study, 41.7% of patients had positive troponin with statistical insignificant difference between groups. According to distribution of patients as regards outcomes, died patient and patients with heart failure had significantly higher median of first- and second-hour CRP than patients without adverse events

Conclusion: Impaired reperfusion was correlated with higher hs-CRP compared to optimal reperfusion. This study was conducted on CRP so further investigation with larger population size are necessary especially for inflammatory cascade.

Keywords: Hs CRP, PCI, STEMI, Thrombolysis.

INTRODUCTION

Acute myocardial infarction (AMI) is potential causative for morbidity as well as mortality worldwide. MI occurs as a result of ischemia of the myocardium, which is a poor blood supply that increases critical threshold, and reduces the cellular repairing mechanism of the myocardium that maintain homeostasis and normal function. Death or irreversible myocardial damage were consequences of prolonged ischemia at this critical threshold level [(1)].

A previous studies reported prognostic improvement in AMI patients. The clinical practice supported clinical trials regarding the potential effect of novel treatments as the recommendations of guidelines improved the prognosis [(2)]. The high sensitivity is the difference between hs-CRP and CRP. CRP levels were measured below 3-5 mg/L, while hs-CRP can be measured down to 0.3 mg/L, which can detect lower inflammatory levels than CRP [(1)].

Hs-CRP blood tests were used for evaluation of the risk of cardiac disease in future, also hs-CRP can help in targeted therapy to intercept cardiovascular disease (CVD). The hs-CRP cut-off point 2 mg/L were used in clinical trial as increased CVD risk, and the normal hs-CRP level is less than 1 mg/L [(3)]. hs-CRP values below 1 mg/L are regarded low risk, while those between 1 and 3 mg/L are considered average, those over 3 mg/L are considered high risk, and hs-CRP levels over 10 mg/L suggest acute inflammation [(4)].

There is probable importance of hs-CRP in the clinical practice as a prognostic value for the success of treatment of STEMI by pharmacological therapy or medical intervention. This importance will benefit us in predicting the outcome and incidence of complications on the short-term-run in STEMI patients. Thus, reducing the morbidity and mortality in patients having coronary artery disease.

This work aimed to clarify the in-hospital prognostic value of hs-CRP in STEMI patients who are treated by thrombolysis vs. primary PCI and comparing the outcome of the treatment between the two groups.

PATIENTS AND METHODS

Forty-eight STEMI cases were divided into two groups in this cross-section study: Patients in group A had primary percutaneous coronary intervention, whereas those in group B received thrombolysis treatment.

Inclusion Criteria: We recruited all the STEMI cases in the period from January 2020 to July 2020 treated by I.V. streptokinase or 1ry PCI.

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Exclusion Criteria: Passed-time MI, contraindications to management, liver failure, cancers, rheumatic arthritis, acute severe infections, and renal impairment.

All cases were subjected to:

1. **Clinical history** and demographic data were collected for all patients at time of hospital admission.
2. **Clinical examination** was done: Vital signs measuring and close monitoring and follow-up. Brief general examination, and full cardiovascular examination: inspection, palpation, and auscultation.
3. **Investigations** were done to confirm STEMI diagnosis and other considered medical issues: ECG. Lab. Tests: CBC, INR, Urea, Creatinine, ALT, AST, Na+, K+, CKMB and serial qualitative and quantitative troponin. Laboratory workup regards hs-CRP: Blood samples from all the patients of the study were collected at time of diagnosis and 24 hours after receiving I.V. Streptokinase or undergoing to 1ry PCI and their quantitative hs-CRP levels were analyzed and measured by the main laboratory of Faculty of Medicine, Zagazig University and/or Suez Health Insurance Hospital using the agreed method. The final data were collected to be statistically analyzed and interpreted.
4. **Imaging:**

-Chest X-ray (CXR) (if needed).

-Echocardiography: was done at time of admission and before discharge and comparing the measured values found especially systolic dysfunctions, segmental wall motion abnormalities and mitral regurgitation grade, if any. Further comparison of the final data of echo findings with the final data of hs-CRP work-up was done to clarify the prognosis.

-Coronary angiography: was done to all patients intended for undergoing 1ry PCI as a line of diagnosis and treatment. All patients had been proceeded upon under local anesthesia of the groin or wrist regions in complete aseptic condition. A diagnostic catheter was introduced upon a diagnostic wire through the femoral or radial artery access after sheath emplacement using modified Seldinger's technique. Multiple different views were taken under fluoroscopy to assess the coronary arterial system after engagement of left and right coronary systems by the suitable diagnostic catheters and injection of the appropriate intracoronary dye. The lesions of the culprit arteries were stented during 1ry PCI procedures using the appropriate instruments and suitable guiding catheters, wires, balloons and stents [(5)].

Ethical consent:

An approval of the study was obtained from Zagazig University Academic and Ethical Committee. Every patient signed an informed written consent for acceptance of participation in the study. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical Analysis

Statistical analysis was carried out utilizing the SPSS version 24. Qualitative data were represented as frequencies and relative percentages and were compared by chi square test (χ^2) or Fisher exact test. Quantitative data were expressed as mean ± SD (Standard deviation), range, median, and interquartile range and were compared by independent samples t-test (parametric data) or Mann-Whitney U test (nonparametric data). P value < 0.05 was considered significant.

RESULTS

There were insignificant statistical differences between both groups regarding age, gender, comorbidities, and family history of CVD (Table 1).

Table (1): Basic data of patients

Characteristics	All patients (n=48)	Group A (n=24)	Group B (n=24)	P-value
Age years (Mean±SD) Range	59.4±6.4 38-73	60.6±5.4 35-73	58.2±7.2 38-73	0.196
Gender				
Male	44(91.7%)	21(87.5%)	23(95.8%)	0.609
Female	4(8.3%)	3(12.5%)	1(4.2%)	
Comorbidities				
DM	31(64.6%)	16(66.7%)	15(62.5%)	
HTN	20(41.7%)	9(37.5%)	11(45.8%)	
Dyslipidemia	15(31.3%)	9(37.5%)	6(25%)	0.680
Family history of CVD				
Yes	27(56.3%)	14(58.3%)	13(54.2%)	
No	21(43.7%)	10(41.7%)	11(45.8%)	0.771

SD= Standard deviation, DM=diabetes mellitus, HTN=hypertension, CVD=cardiovascular disease

Most of patients had grade II mitral regurge and wall motion abnormalities in anterior septum with insignificant statistical difference between groups (Table 2).

Table (2): ECG and ECHO parameters in the study groups

Findings	All patients (n=48)	Group A (n=24)	Group B (n=24)	P-value
LBBB	5 (10.4%)	2 (8.35)	3 (12.5%)	0.975
ST	10 (20.8%)	5 (20.8%)	5 (20.8%)	
ST (V1-V5)	11 (22.9%)	5 (20.8%)	6 (25%)	
ST (aVF)	13 (27.1%)	7 (29.2%)	6 (25%)	
ST (V1-V4)	9 (18.8%)	5 (20.8%)	4 (16.7%)	
EF% mean±SD	53±6.7	51±5.4	54±7.5	0.119
SWMA				0.979
Anterior septal hypokinesis	21(43.8%)	10(41.7%)	11(45.8%)	
Anterolateral septal hypokinesis	7(14.6%)	4(16.7%)	3(12.5%)	
Inferolateral septal hypokinesis	12(25%)	6(25%)	6(25%)	
Septal hypokinesis	8(16.7%)	4(16.7%)	4(16.7%)	
MR grades				0.891
Trivial	10(20.8%)	5(20.8%)	5(20.8%)	
I	5(10.4%)	2(8.4%)	3(12.5%)	
II	33(68.8%)	17(70.8%)	16(66.7%)	

SD= Standard deviation, LBBB=left bundle branch block, ST=ST segment, EF=ejection fraction, SWMA= segmental wall motion abnormalities, MR=mitral regurge

In group A, most of patients underwent PCI in LAD (58.3%), while in RCA (20.8%) and in LCX (4.2%) as shown in figure 1.

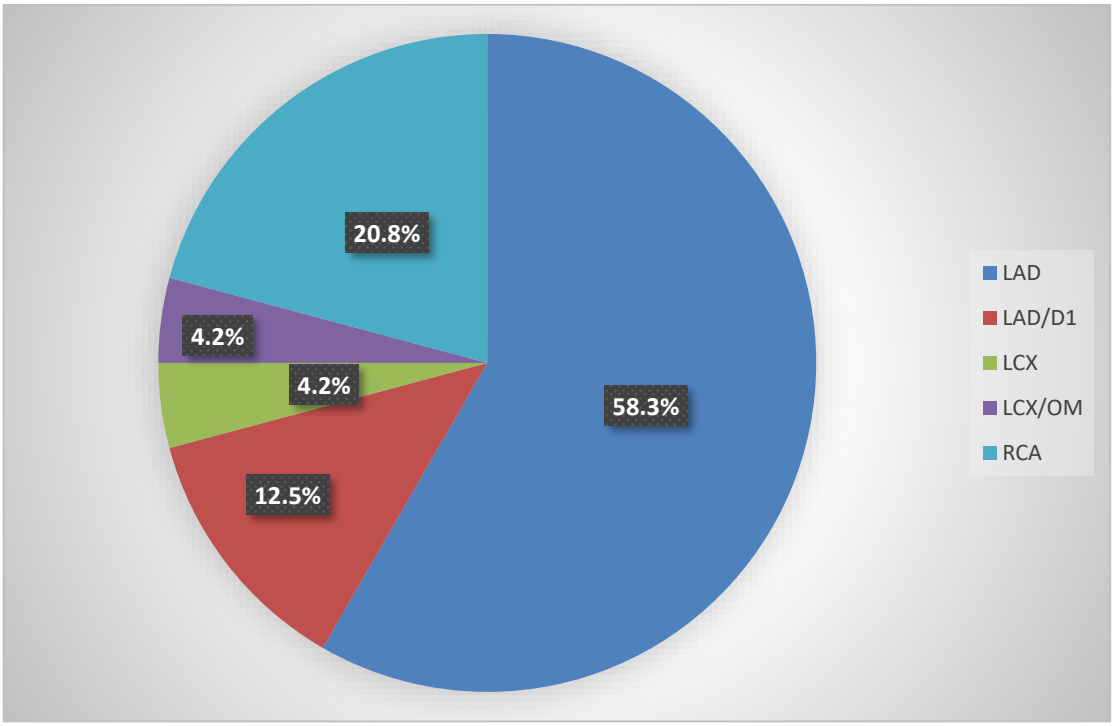

Figure (1): Distribution of artery of PCI

In table 3 one patient died in group A and two patients had heart failure.

Table (3): Major adverse cardiovascular events in the study groups

MACE	All patients (n=48)	Group A (n=24)	Group B (n=24)	P-value
Heart failure	2 (8.4%)	2 (8.4%)	0 (0%)	0.489
Death	1 (4.2%)	1 (4.2%)	0 (0%)	1.00

In table 4, according to distribution of patients as regards outcomes, died patient and patients with heart failure had significantly higher median of first and second hour CRP than patients without adverse events.

Table 4: Laboratory findings in groups according to outcome

Findings	No MACE (n=45)	Died patient (n=1)	Heart failure patients (n=2)	P-value
Troponin				
Positive	20 (44.4%)	0 (0%)	0 (0%)	
Negative	25 (55.6%)	1 (100%)	2 (100%)	0.504
CKMB				
Median (IQR)	36.3 (7)	34 (3)	30 (2)	0.443
1st hour-CRP				
Median (IQR)	15 (21)	97.58 (55)	95 (53)	**<0.001***
2nd hour-CRP				
Median (IQR)	25 (27)	157.43 (62)	96 (49)	**<0.001***

MACE =Major adverse cardiovascular events, IQR= Interquartile range

DISCUSSION

The current study assessed hs-CRP prognostic role regarding the incident of major adverse cardiac events (MACE) in cases with AMI treated with PCI versus thrombolysis. No statistical significant difference between hs-CRP was found in the study patients. The hs-CRP was elevated in dead cases with heart failure. Based on the hypothesis, our findings reported that regarding AMI cases, the increased levels of hs-CRP correlated with inflammatory events caused by myocardial disease, while in cases with unstable angina the CRP increased levels were correlated with recurrent infarctions and plaque instability. Regarding ACS and ST-elevation, the heart failure and mortality were related to increased CRP [6].

Our study were in accordance with a systemic review, that elevated CRP levels were correlated with elevated mortality and MACE of in-hospital follow-up and recurrent MI [7]. **Wada *et al.*** [8] reported that hs-CRP before procedure was correlated with MACE and death's all-cause in cases with PCI during follow-up median of 6.5 years. **Kang *et al.*** [9] showed that hs-CRP was predicting independently for 36-month follow-up of MACE, and during the first 6 months, in cases with acute MI after PCI with high statin intensity, these findings support the statins anti-inflammatory effect.

Park *et al.* [10] found that concerning the stent thrombosis, hs-CRP was a potential predicting agent (HR 3.86; 95% CI 1.82–8.18; $p < 0.001$), and report significant role of inflammation in this event. Canakinumab an interleukin-1β monoclonal antibody, performed a potential decrease of cardiovascular recurrent events, and hs-CRP, which reported by a study[11]. **Suleiman *et al.*** [12] in a largescale study with follow-up of 23 months, reported a correlation between high mortality rate and after hospital-discharge and CRP.

The prognostic role of CRP remained unclear in primary PCI (pPCI) treatment of STEMI. This unclear event caused by attributed reports and inconsistency of information in previous reports. **Tomoda and Aoki** [13] in a study conducted in 234 STEMI cases with pPCI and stenting, CRP level over 0.3 mg/dL was a predictor agent of target-vessel revascularization, in-hospital coronary reocclusion, and death. The failure of sensitive method to detect CRP, retrospective design, failure of exclusion of cases with inflammatory diseases or using anti-inflammatory medication, and failure to use modern tools for percutaneous intervention, were limitations in this study.

Another study revealed that hs-CRP was correlated with target-vessel revascularization, AMI, long- and short-term death [14]. Because of the lack of admission CRP data, a substantial percentage of cases were excluded from the cohort in this retrospective investigation (22 percent of the original sample).

Kruk *et al.* [15] though there were no exclusion criteria, hs-CRP was found to be a predictor of in-hospital death.

CONCLUSION

We found that hs-CRP was predictive of composite MACE in patients who underwent primary angioplasty and stenting. Impaired reperfusion is also associated with higher hs-CRP levels compared to optimal reperfusion.

Hs-CRP is one of many markers in the inflammation network and must be studied in conjunction with others. Other inflammatory indicators and their trajectory following treatment for STEMI are interesting to investigate further.

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