# Relationship between Serum Level of High-Sensitive C-Reactive Protein and Extension of Myocardial Involvement in Patients with Acute Myocardial Infarction

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**Introduction**. The high-sensitive C-reactive protein (HS-CRP) assay is being increasingly used as a marker for cardiac risk assessment and as a prognostic tool in heart disease. In current study, we assessed the relationship between serum level of HS-CRP and extension of myocardial involvement in acute myocardial infarction.

**Methods**. In a Cross-Sectional study, 50 patients with the final diagnosis of acute myocardial infarction and admitted for the first time in CCU wards of the Kerman University in 2010 were studied. Serum HS-CRP and Troponin I level was measured using commercial ELISA kits, 24 hours after the appearance of first manifestations. All patients underwent 2-dimensional echocardiography for assessing the number and severity of involved segments as well as wall motion abnormality.

**Results**. There was a strong positive correlation between the serum level of HS-CRP and serum Troponin I level ($\beta = 0.509$, $p < 0.001$). Multivariable linear regression showed that the level of HS-CRP could strongly predict serum level of Troponin I within the first 24 hours of MI appearance (Beta = 0.308, Standard Error = 0.080, $p < 0.001$). But, no significant relationships were revealed between the mean serum HS-CRP level and the location of myocardial infarction, the number of involved segments, left ventricular ejection fraction, and ST-segment elevation score.

**Conclusion**. For a strong correlation between HS-CRP and Troponin I, HS-CRP can be a useful biomarker for predicting extended myocardial involvement in patients with acute myocardial infarction.

**Key words**: Myocardial infarction, C-reactive protein, Troponin, Risk.

The high-sensitive C-reactive protein (HS-CRP) assay is a quantitative analysis test that is increasingly used as a marker for cardiac risk assessment as well as a prognostic tool in heart disease [1]. This test, in addition to lipid evaluation and global risk scoring systems, helps in the evaluation of cardiovascular disease risk. HS-CRP is an acute phase protein that appears in circulation in response to inflammatory cytokines, such as interleukin-6, and serves as a biomarker for systemic inflammation [2][3].

With the recognition of the crucial link between arterial damage, inflammatory processes, and coronary atherosclerosis, HS-CRP estimation has assumed a vital role in cardiac risk assessment and therefore its effects as an important pathogenic factor for inducing atherosclerosis and other reactions involved in atherothrombogenesis is clearly proved [4-7]. Following a systematic review of the association between inflammatory markers and coronary heart disease and stroke, the American Heart Association (AHA) and Centers for Disease Control and Prevention (CDC) developed a scientific statement that recommends HS-CRP as a more sensitive assay for the prediction of vascular disease, compared to traditional assays for circulating C-reactive protein levels [8][ 9].

Although the HS-CRP assay has been recommended in patients with intermediate risk of coronary heart disease in order to determine the need for further evaluation and therapy, its relationship with extension and severity of ischemia following myocardial infarction is already questioned. Also, the role of HS-CRP measurement for discriminating ischemia and non-ischemic situations as well as its correlation with the different myocardial infarction indicators such as cardiac enzymes and echocardiographic parameters is unclear.

In this study, we assessed the relationship between serum level of HS-CRP and extension of myocardial involvement in patients with acute myocardial infarction.

## MATERIALS AND METHODS

### Study population

In a cross-sectional study, 50 consecutive patients (mean age 60.62 ± 11.81, range: 33 to

85 year; 70.0% Male) with the final diagnosis of acute myocardial infarction and admitted for the first time in CCU wards of the city of Kerman in 2010 were studied. Patients had the following criteria: 1) typical chest pain lasting ≥30 min; 2) ST-segment elevation ≥0.2 mV in ≥2 contiguous precordial leads (for the diagnosis of anterior wall MI) or in leads $V_1$–$V_3$ (for the diagnosis of anteroseptal wall MI) as well as ≥0.1 mV in II, III, and aVF leads (for the diagnosis of inferior wall MI) on the admission ECG; 3) increase in serum creatine kinase (CK) level more than twice the normal value. Those with the history of renal dysfunction (serum creatinine > 1.5 mg/dL), recent acute coronary syndrome, valvular heart disease, life-threatening arrhythmias, acute or chronic liver disease, non-coronary inflammatory or infectious disorders or symptomatic heart failure were excluded. Baseline characteristics of the participants were collected from the recorded files of the hospitals and by face to face interviewing the patients or their families, including demographics, medical history, clinical manifestations, and medication.

### Study measurements

Venous blood samples were obtained 24 hour after the admission time. Serum HS-CRP and Troponon I levels were measured using commercial ELISA kits (Monobind, USA), 24 hours after the appearance of first clinical manifestations using the ELIZA method. All measurements were performed in a single hospital laboratory. All patients underwent 2-dimensional echocardiography by a cardiology resident and under-supervision of a cardiologist for assessing number and severity of involved segments as well as wall motion abnormality and for rule outing other non-ischemic and valvular diseases.

## STATISTICS

Data were presented as mean ± SD for continuous variables and percentages for categorical variables. Comparisons of categorical variables were performed using an overall chi-square test or Fisher's exact test if required; while comparisons of continuous variables were performed using an independent t-test or ANOVA test. A linear correlation between the variables was determined by the Pearson's correlation coefficient test. Receiver operator characteristic (ROC) curves were constructed to investigate the power of HS-CRP level for discriminating involved and non-involved myocardial situations. Predictors exhibiting a statistically significant relation with HS-CRP level in univariate analyses were taken for multivariate linear regression analysis to investigate their independence as predictors. Beta and 95% confidence intervals (CI) for beta were calculated. This study was done with the power of 90%. P values of 0.05 or less were considered statistically significant. All the statistical analyses were performed using SPSS version 13.0 (SPSS Inc., Chicago, IL, USA) and SAS version 9.1 for Windows (SAS Institute Inc., Cary, NC, USA).

## RESULTS

In a current study, 50 patients (mean age 60.62 ± 11.81, range: 33 to 85 year; 70.0% Male) with acute myocardial infarction were entered into the study. No significant differences were observed between men and women regarding mean age (59.74± 11.45 *versus* 62.67± 12.78, p = 0.452). Acute myocardial infarction has commonly appeared in inferior wall in 42% of the participants, followed by anteroseptal wall MI that has occurred in 36% of the patients. Anterior and inferolateral wall involvements have also appeared in 14% and 8% of them, respectively. There was also no significant difference in the location of MI between the two genders (p = 0.982) (Table I). With respect to the number of involved segments, 3 segments were involved in 56%, 4 segments were involved in 16%, 5 segments were defected in 20%, and 6 segments were affected in 8% of the patients. Men and women were similar in term of the involved segments following acute MI (P = 0.362). The mean of serum Troponin level in the study patients was 13.43 ± 7.75 mg/L that was similar in men and women (men: 13.87 ± 8.26, women: 12.41 ± 6.53 mg/L, p = 0.508). The mean of serum HS-CRP level in the study patients was 19.54 ± 12.15 mg/L that was similar in men and women (men: 19.39 ± 12.59, women: 19.88 ± 11.46 mg/L, p = 0.895). The mean of ST-segment elevation score in the patients was 7.76 ± 2.77 percent that only 7 (14%) had a score more than 10. Men and women had statistically similar mean ST-segment elevation score (men: 7.51 ± 2.72, women: 8.33 ± 2.90, p = 0.359).

There was a strong positive correlation between the serum level of HS-CRP and serum Troponin level (β = 0.509, p < 0.001). But, no significant correlations were observed between the serum level of HS-CRP and two parameters of LV ejection fraction (β = -0.058, p = 0.687) and ST-

segment elevation score (β = 0.063, p = 0.664). Also, no significant relationship was revealed between the mean serum HS-CRP level and the location of myocardial infarction (Inferior wall: 19.49 ± 12.84, Anteroseptal wall: 18.33 ± 11.67, Anterior wall: 22.84 ± 13.59, inferolateral wall: 19.48 ± 11.61, p = 0.881). No significant relationship was also found between the mean serum HS-CRP level and the number of involved segments (three segments: 18.90 ± 12.51, four segments: 24.64 ± 12.40, five segments: 16.53 ± 10.25, six segments: 22.75 ± 14.45, p = 0.499).

Multivariable logistic regression model with the presence of the variables of gender, sex, and location of MI (Table II) showed that the level of HS-CRP could strongly predict serum level of Troponin within the first 24 hours of MI appearance (Beta = 0.308, Standard Error = 0.080, p < 0.001). According to the ROC curve analysis, serum HS-CRP measurement was an acceptable indicator of Troponin level > 10 and therefore severe ischemia status with areas under the ROC curves 0.895 (95% CI: 0.806 – 0.984, p < 0.001).

*Table I*
Baseline characteristics of the study patients

| Characteristics | Total (n = 50) | Men (n = 35) | Women (n = 15) | P-value |
|---|---|---|---|---|
| Age (year) | 60.62 ± 11.81 | 59.74± 11.45 | 62.67± 12.78 | 0.452 |
| Location of acute MI *: | | | | |
| Inferior | 42.0% | 42.9% | 40.0% | |
| Anteroseptal | 36.0% | 34.3% | 40.0% | 0.982 |
| Anterior | 14.0% | 14.3% | 13.3% | |
| Inferolateral | 8.0% | 8.6% | 6.7% | |
| Number of involved segments: | | | | |
| Three | 56.0% | 48.6% | 73.3% | |
| Four | 16.0% | 17.1% | 13.3% | 0.362 |
| Five | 20.0% | 25.7% | 6.7% | |
| Six | 8.0% | 8.6% | 6.7% | |
| Serum Troponin I level (mg/L) | 13.43 ± 7.75 | 13.87 ± 8.26 | 12.41 ± 6.53 | 0.508 |
| Serum HS-CRP † level (mg/L) | 19.54 ± 12.15 | 19.39 ± 12.59 | 19.88 ± 11.46 | 0.895 |
| LV ejection fraction (%) | 40.83 ± 7.74 | 40.83 ± 7.74 | 45.00 ± 6.81 | 0.067 |
| ST-segment elevation score | 7.76 ± 2.77 | 7.51 ± 2.72 | 8.33 ± 2.90 | 0.359 |

* Myocardial infarction
† High-Sensitive C-Reactive Protein

*Table II*
Relationship between serum HS-CRP and Troponin I levels with the presence of probable cofounders

| Variable | Beta | Standard Error | P-value |
|---|---|---|---|
| HS-CRP level | 0.308 | 0.080 | < 0.001 |
| Male gender | -1.782 | 2.087 | 0.398 |
| Age | 0.104 | 0.083 | 0.217 |
| Location of MI | 1.285 | 1.062 | 0.233 |

R-Square = 0.311
† High-Sensitive C-Reactive Protein

## DISCUSSION

In this cross-sectional study, the relationship between the measure of serum HS-CRP level and extension and severity of cardiac ischemia in patients who suffered from acute myocardial infarction was assessed. On the other hand, a correlation between different scores of infarct size with the biomarker of HS-CRP was studied. We considered some indicators for evaluating infarction severity including serum Troponin I level, ST-segment elevation score, number of involved segments in echocardiography and left ventricular ejection fraction. However, we revealed only a strong association between HS-CRP level and serum Troponin I. This correlation even proved in a multivariable regression model with probable confounders. Biochemical markers are useful for predicting future cardiovascular events in patients with acute coronary syndrome. Especially, HS-CRP rise has been reported before as well as during unstable angina episodes even in the absence of evidence of myocardial injury [10][11]. The independent as well as the combined prognostic value of elevated Troponin-I and HS-CRP on myocardial infarction risk score and on the short-

term prognosis were demonstrated in some previous studies and showed that the use of HS-CRP and Troponin-I in combination appears to add critical prognostic insight to the assessment of patients with myocardial infarction [12,13]. But in the present study, we focused on the value of HS-CRP for predicting severe and extended infarction from mild ischemic status. The correlation between this biomarker and Troponin I enzyme has been also shown in some studies. In a study by Munk and colleagues, the mean and the sum of CRP values per week were significantly correlated with the number of patients with a Troponin $\geq 0.03$ µg/l in the same week. In fact, our study supported the hypothesis that inflammation assessed by CRP levels is linked to the prospective development of cardiovascular events manifested by increased Troponin enzyme [14].

Regarding relationship between Troponin I enzyme and inflammatory markers such as HS-CRP, some animal studies demonstrated that provocation of an autoimmune response to mc-TnI induces severe inflammation in the myocardium followed by fibrosis and heart failure with increased mortality in mice. It was suggested that the mice immunized with Troponin I developed severe inflammation of the myocardium with increased expression of inflammatory chemokines regulated on activation normal T cell expressed and secreted, monocyte chemoattractant protein-1, macrophage inflammatory proteins, T-cell activation gene 3, and eotaxin and chemokine receptors. Furthermore, it was demonstrated that mice preimmunized with Troponin I before left anterior descending coronary artery ligation showed greater infarct size, more fibrosis, higher inflammation score, and reduced fractional shortening [15]. Although animal studies could show the role of Troponin I for inducing inflammatory processes and thus increasing inflammatory markers such as CRP in cardiac tissues following injury and ischemia, this relation was not completely proved in clinical studies and need to be more investigated.

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*Test de mare sensibilitate a proteinei C reactivă (CRP-HS); testul este tot mai mult folosit ca un marker pentru evaluarea riscului cardiac şi ca un instrument de prognostic în bolile de inimă. În stadiul actual, am evaluat relaţia dintre nivelul seric al HS-CRP şi extinderea de implicare miocardică în infarctul miocardic acut.*

***Metode**. Într-un studiu transversal, 50 de pacienţi cu diagnosticul final de infarct miocardic acut şi recunoscut pentru prima dată în secţii CCU de la Universitatea Kerman în 2010 au fost studiate. Serul de HS-PCR şi nivelul de Troponina au fost măsurate cu ajutorul kiturilor comerciale ELISA, la 24 de ore după apariţia primelor manifestări. Toţi pacienţii au fost evaluaţi ecocardiografic 2D pentru a evalua numărul şi severitatea leziunilor pe segmente implicate, precum şi mişcări anormale de perete.*

***Rezultate**. A existat o corelaţie puternic pozitivă între nivelul seric al HS-CRP şi nivelul troponinei serice I ( $\beta = 0.509$, $p<0.001$). Regresia multivariabilă liniară a arătat că nivelul de CRP HS ar putea prezice puternic nivelul seric al troponinei I în primele 24 de ore de la apariţia infarctului miocardic ( $\beta = 0.308$, Eroare standard = 0.080, $p<0.001$). Dar, nu au fost descoperite relaţii semnificative între valoarea medie a nivelului seric de HS-PCR şi locaţia de infarct miocardic, numărul de segmente implicate, fracţia de ejecţie a ventriculului stâng, şi ST-segment.*

***Concluzie**. Pentru o corelaţie puternică între CRP-HS şi troponina I, HS-PCR poate fi un biomarker util pentru estimarea implicării extinse a miocardului la pacienţii cu infarct miocardic acut.*

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