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# Relationship between serum CRP level and left ventricular function in patients with acute ST–elevation myocardial infarction: A cross–sectional study

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## ABSTRACT

**Objective:** To investigate the relationship between serum C-reactive protein (CRP) level and left ventricular function in patients with acute ST-elevation myocardial infarction.

**Methods:** This study is a descriptive-analytic study and was conducted on patients with ST-elevation myocardial infarction, who were admitted to the Urmia Hospital in Seyed Alshohada Hospital, and underwent primary percutaneous coronary intervention from October to March 2018. Demographic, angiographic, echocardiographic data were evaluated based on the patients' records. All patients were evaluated for 90 min and CRP levels were measured during the first 6 h after the primary percutaneous coronary intervention.

**Results:** A total of 114 patients were studied, among whom 71.9% (82 patients) were male, and their mean age was (57.86±9.57) years old. The mean BMI was (26.1±3.8) kg/m<sup>2</sup>. Altogether 38.6% (44 patients) had a history of smoking, 17.5% (20 patients) of diabetes, 38.6% (44 patients) of hypertension, 5.3% (6 patients) of hyperlipidemia and 7.0% (8 patient) of coronary artery disease. The results showed a significantly negative correlation between ejection fraction and CRP, left atrial volume and CRP ( $P<0.05$ ), and a significantly positive correlation between the global longitudinal strain level and CRP. The CRP level was significantly different at various diastolic grades ( $P=0.001$ ). The level of CRP in patients with grade 2 diastolic dysfunction was higher than grade 1 diastolic dysfunction, while the level of CRP in diastolic grade 1 diastolic dysfunction was higher than the normal function.

**Conclusions:** High CRP levels are associated with ejection fraction, global longitudinal strain loss and left atrial volume.

**KEYWORDS:** Coronary artery disease; ST elevation myocardial infarction; C-reactive protein; Myocardial infarction

## 1. Introduction

Today, cardiovascular disease (CVD) including acute myocardial infarction is the most common cause of death in the world[1]. According to the latest global study, more than 422 million people suffer from CVD, and the disease kills over 17 million deaths annually[2]. Diagnosis of acute myocardial infarction is based on the clinical symptoms, electrocardiographic changes, and elevated cardiac enzymes[3]. There are two types of myocardial infarction: ST-segment elevation myocardial infarction (STEMI) and non-ST elevation myocardial infarction (NSTEMI), and each one has a specific treatment strategy. Two treatment strategies are effective for STEMI. *i.e.*, angiography and thrombolytic therapy[4]. According to the recent guidelines, primary percutaneous coronary intervention (PPCI) is the gold standard for the treatment of STEMI patients[3]. PPCI refers to PCI in the case of STEMI when patients do not receive fibrinolytic therapy within 12 h of symptom onset. Compared to fibrinolytic, PPCI is associated with high openness of the involved vein, reduction of ischemia recurrence, and reduction of complications such as re-infarction, death, intracerebral hemorrhage, *etc.* For patients who need PPCI, the pre-procedure

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measurement of C-reactive protein (CRP) can help to identify high-risk patients[5]. Identifying the risk factors for coronary heart disease such as hypertension, diabetes, insulin resistance, dyslipidemia, positive family history, smoking, fibrinogen restriction, lipoprotein, and inflammatory markers is important for managing this disease[6]. In recent decades, it is strongly advocated to regard atherosclerosis as an inflammatory disease, therefore, serum levels of inflammatory markers (including CRP) have been taken into consideration to determine the risk of cardiovascular cases[7,8].

Numerous studies have shown that CRP markers are elevated in myocardial infarction patients and are associated with the severity and complications (such as heart failure or remodeling)[9-11]. CRP is an accelerating or exacerbating factor of acute coronary diseases such as myocardial infarction, and the underlying mechanisms are not exactly known. Some researchers have shown that CRP is likely to trigger inflammation in atheromatous plaque or cause rupture or bleeding in the plaque by activating the complement, and it is still unknown whether there is a direct relationship between CRP level and the severity of the injury[12,13].

Some studies have suggested CRP as a predictor of vascular events such as stroke, myocardial infarction, and peripheral vascular obstruction among healthy people, the elderly people and smokers[14,15]. In patients with acute coronary artery disease or post-myocardial infarction, elevated CRP levels may indicate re-instability. This marker may even serve as a sensitive predictor for future cardiovascular events in healthy individuals[16].

Prolonged inflammation in patients with STEMI can also cause many complications, including loss of myocytes, reduction in left ventricular systolic function, dilation of heart cavities, loss and even rupture of ventricular wall integrity. As noted by Zacho *et al.*, activation of the innate immune system by acute-phase proteins such as CRP in patients with coronary artery disease can lead to cellular damage, activation of complement and the aforementioned injuries[17]. One study has shown that it also causes cardiac dysfunction in addition to increasing infarct size[18].

To date, many studies explored the impact of elevated CRP levels on patients undergoing PCI selectively (stable or unstable angina) or following NSTEMI[19]. However, only a few addressed the predicting role of CRP in patients with PPCI following STEMI. On the other hand, the presence of echocardiographic criteria, especially diastolic or systolic dysfunction of the left ventricular following myocardial infarction and elevated left ventricular filling pressure can lead to adverse clinical complications and decreased survival rate[20,21]. The present study investigated the CRP level at the baseline and left ventricular dysfunction in patients with STEMI who underwent successful PPCI. It was assumed that patients with high CRP levels were more likely to suffer from ventricular dysfunction. The aim of the present study was to investigate the relationship between serum CRP level and left ventricular function in patients with STEMI and to investigate the role of inflammatory factors in STEMI patients undergoing PPCI.

## 2. Materials and methods

### 2.1. Design

This cross-sectional study was performed on 114 patients with STEMI who underwent PPCI at Seyyed al-Shohada Hospital, Urmia from October to March 2018. The sample size was estimated 100 individuals based on previous studies, taking into account a lower error rate of less than 0.05, test power of 90%, 95% confidence interval, total patients ( $n=3\ 000$ ), STEMI prevalence of 2.5% in Iran. To increase data reliability, 114 individuals were included in the study.

### 2.2. Participants

All patients who met the inclusion criteria were included in the study using a convenience sampling method. Data were collected using checklists, including demographic, angiographic and echocardiographic data. STEMI diagnosis was made based on a typical history of chest pain, electrocardiographic changes (greater than 1 mm increase in the two adjacent leads) and elevated levels of cardiac biomarkers[22]. PPCI was carried out in all patients within 90 min and CRP levels were measured within the first 6 h[23].

The inclusion criteria of this study included (1) Patients with STEMI and referred to the center; (2) Patients over 75 years of age (to avoid the effect of age-related diastolic disorder); (3) Patients with a history of previous myocardial infarction were included. The exclusion criteria were as follows: (1) Having history of STEMI; (2) Patients who were on cardiogenic shock at baseline (pressure less than 90 mmHg that does not respond to inotrope or fluid therapy); (3) Patients with creatinine level  $\geq 1.2$  mg/dL; (4) Liver problems with higher than 2-fold increase in liver enzymes; (5) Patients with advanced cancer; (6) Patients with a previous history of liver failure, rheumatologic diseases or infectious diseases.

### 2.3. Indexes measurement

CRP levels were measured using Bayer wide-range kits[24]. Echocardiography was also performed by echocardiographic devices, including Medison, Vidid 6, Siemens, and Vivid 3. All echocardiographic criteria mentioned in the table of variables [ejection fraction, mitral cellulitis, E/E', pulmonary hypertension, isovolumic relaxation time, global longitudinal strain, left ventricle (LV) volume, and left atrial (LA) volume] were measured. Finally, based on the CRP level all patients were divided into three groups:  $<2.6$  mg/L, 2.6-7.9 mg/L, and  $>7.9$  mg/L[25]. The data were recorded and CRP levels were checked for each patient individually.

## 2.4. Ethical consideration

This study was approved by the Ethics Committee of Urmia University of Medical Sciences and the Ethics Committee of the place where the research was conducted (Ethic code: IR.UMSU.REC.1397.370). The Strengthening the Reporting of Observational studies in Epidemiology (STROBE) checklist was used to report the study. Oral and written consent was obtained from all participants.

## 2.5. Data analysis

The data were analyzed using SPSS ver. 22. Measurement data were expressed as mean±SD, while categorical data were expressed as percentages. Categorical (qualitative) variables were analyzed using *Chi*-square test, and measurement data by one-way ANOVA followed by Duncan's *post hoc* test. The significance level of the tests was set at  $\alpha=0.05$ .

## 3. Results

The present study was performed on 114 patients with STEMI. The mean age of participants was (57.86±9.57) years (range: 36-74 years). Most participants were male (71.9%) and the BMI of males was 26.14 and it was 27.1 for females. A total of 38.6%, 17.5%, 38.6%, 5.3%, 3.5%, 1.8% and 7.3% of patients had history of hypertension, diabetes, smoking, dyslipidemia, asthma, COPD, and CVD, respectively. Most participants had no diastolic disorder. The location of infarction in most participants was the anterior part of the heart (56.1%). The most involved artery was left anterior descending artery (LAD) (56.1%). The mean CRP level was (14.75±15.79) mg/L. The mean ejection fraction (EF) level was (39.35±8.96)%. Velocity of mitral valve level was 0.85±0.08. E/e level was 0.09±0.02. Pulmonary hypertension was (22.8±4.3) mm Hg. Isovolumic relaxation time (IVRT) ratio was (101.63±16.28) msec. LV volume level was (93.88±23.96) mL. LA level was (44.67±12.03) mL, and global longitudinal strain level was -12.85±3.23.

The results of the Pearson test showed a significant inverse relationship between EF and CRP level ( $R^2=0.082$ ,  $P<0.05$ ) (Figure 1); A significant positive relationship between GLS and CRP level ( $R^2=0.106$ ,  $P<0.05$ ), so that any decrease in the GLS level (indicating a decrease in left ventricular function) leads to an increase in CRP level (Figure 2); A significant inverse relationship between LA volume and CRP ( $R^2=0.011$ ,  $P<0.05$ ) (Figure 3). The CRP level was significantly different at various diastolic grades ( $P=0.001$ ). CRP level in the diastolic grade 2 (7.9 mg/L) is higher than the diastolic grade 1 (2.6-7.9 mg/L) and the normal (2.6 mg/L).

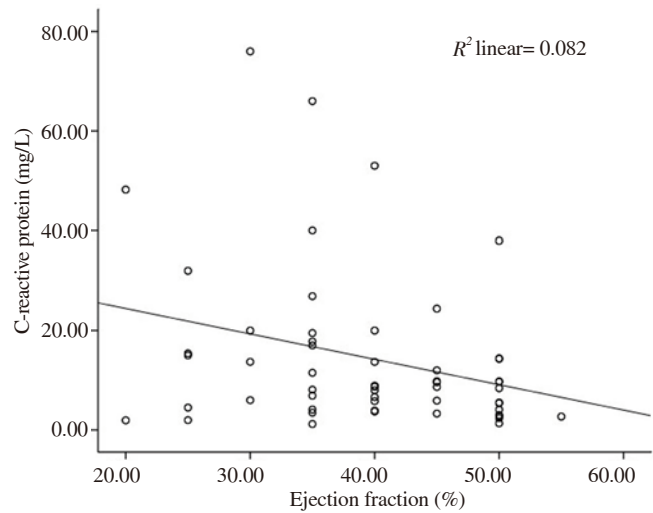


Figure 1. Relationship between cardiac pumping and C-reactive protein levels.

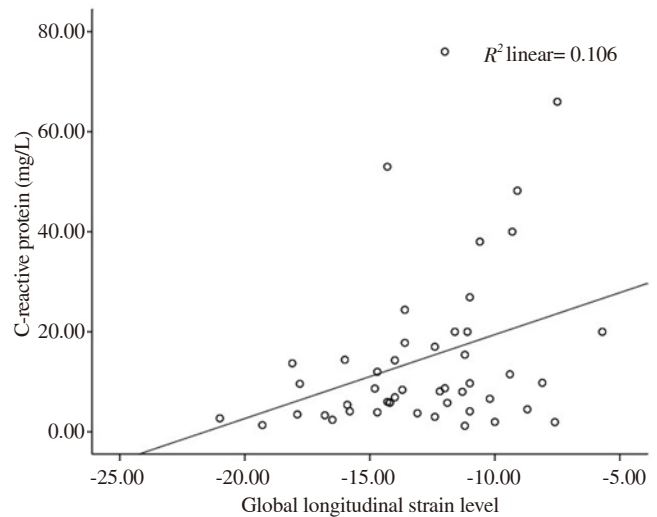


Figure 2. Relationship between left ventricular total dilation values and C-reactive protein levels.

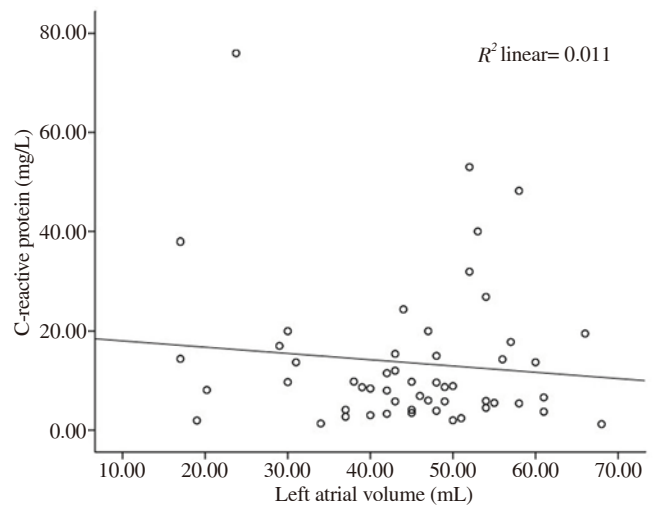


Figure 3. Relationship between cardiac pumping and C-reactive protein levels.

#### 4. Discussion

CRP is an acute-phase protein that is produced primarily in the liver. For many years, CRP has been used as a marker for systemic inflammation. However, recent findings suggest CRP should serve more than an inflammatory marker[3]. CRP may trigger complement activation and poor cardiac remodeling in the cases of ischemic injury. This protein has been found on cells in following myocardial infarction[26]. Many animal studies have shown that CRP significantly increases the extent of myocardial infarction-induced injury in the ischemic region[18,23,27]. Most patients in the present study were male, with an average age of 58 years, which is similar to some studies[22,25,28,29]. It may indicate that men over the age of 60 are at higher risk of coronary heart diseases so that we should pay more attention to this group of people.

The history of smoking, diabetes, hypertension, hyperlipidemia, and family history of coronary heart diseases are the most effective risk factors in most studies[28-30]. With regard to BMI, Jeong *et al.* reported that patients' BMI was 24 kg/m<sup>2</sup>, and there was no significant relationship between CRP and BMI[24]. Further research is needed in this regard.

The most common location of infarction was anterior and posterior regions. LAD and right coronary artery (RCA) were also the commonly involved arteries. Stumpf *et al.* also proved that the common involved artery was LAD followed by RCA and left circumflex artery (LCX). The most common location of the infarction was the anterior and then posterior regions[28], while it is also reported as the anterior region of the heart in another study[25]. The high prevalence of anterior infarction and LAD involvement indicates the importance of this cardiac region.

The results of the present study showed no significant relationship between mitral inflow velocity, E/E' ratio, pulmonary hypertension, IVRT, left ventricular volume or LA volume with CRP levels. In contrast, Shacham *et al.* showed that patients with higher CRP levels had a higher septal E/e ratio. Mean mitral E- and e/e wave velocity, and pulmonary arterial pressure were high, but the study also showed that there was no significant difference in atrial and left ventricular volume[25], which is consistent with our study. The results of Karpi ski *et al.* study showed a significant inverse relationship between CRP, EF, IVRT, and DT levels and a significant positive association between CRP and E/A and E/Ep[31]. In contrast, the results of a study by Arruda-Olson *et al.* are consistent with our study. They showed no relationship between mitral flow velocity, pulmonary hypertension, and LA volume with CRP levels[32]. Different results may be achieved depending on the type of patients selected (patients with reduced or retained EF[23]). However, these inconsistencies indicate the need for extensive matched studies.

Our results demonstrated that the CRP level was significantly different in various diastolic grades. The CRP level was higher in grade 2 diastolic disorder than grade 1 diastolic disorder, and

grade 1 diastolic disorder higher than the normal diastolic function. One study showed that patients with higher CRP levels presented more advanced diastolic dysfunction (higher ventricular filling pressure)[25]. Karpiński *et al.* also reported that elevated CRP levels were associated with more advanced diastolic dysfunction[31]. In myocardial infarction patients, the extent of left ventricular relaxation and thus the extent of ventricular filling in the diastolic phase (even mitral valve function) may be impaired due to impaired movement of some walls under ischemia, elevated left ventricular filling pressure, and some physiological changes[25,32]. Therefore, the result of diastolic dysfunction in the present study is justified, and increased CRP levels led to an increase in diastolic dysfunction. There was a significant inverse relationship between EF and CRP level, and a significant association between GLS with CRP level. It showed left ventricular function in different ways and emphasized that CRP levels increase with a decrease in the left ventricular function in the case of myocardial infarction. Many studies have also emphasized the above finding, but have not investigated the extent of left ventricular dilatation[22,24,29]. However, one study revealed no significant relationship between EF and CRP[23]. Most studies confirmed the association of high CRP levels with low EF, and this inconsistency needs further investigation. In addition, CRP levels predict the progression of heart failure, mortality rates, and rates of major adverse cardiovascular events, which can predict long-term mortality as an independent factor. This marker also demonstrates the potential of biomarkers and shows the severity and number of vessels involved in patients with myocardial infarction[3,25,28,30,33,34].

The results of the present study showed that high CRP levels are associated with greater EF and GLS decline as well as higher grades of diastolic disorder, but are not related with other echocardiographic parameters such as mitral flow velocity, pulmonary artery pressure, IVRT, LA volume, and LV volume. However, considering the limited number of patients and the type of study, as well as the critical role of CRP in patients with myocardial infarction, further research is needed.

#### Conflict of interest statement

The authors report no conflict of interest.

#### Authors' contribution

A.S. and R.A: concept and design, P.I. performed the data collection; A.S. analyzed the data; A.S, P.I and R.A. wrote the paper.

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