

## THE RELATIONSHIP BETWEEN SERUM LEVELS OF HS-CRP AND CORONARY LESION SEVERITY

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### Abstract

**Background and aim.** It is very important to know the risk factors of coronary artery disease and the role of inflammatory markers. One of these markers is hs-CRP that has been indicated to increase in patients with coronary artery atherosclerosis. The main objective of this study was to determine the relationship between serum levels of hs-CRP and coronary lesion severity.

**Methods.** In the current study, we evaluated the role of hs-CRP in coronary artery disease and measured the relationship between serum hs-CRP levels and the severity of coronary lesions in 102 patients who referred to Imam Khomeini Hospital, Iran. The number of involved coronary arteries was measured. The severity of coronary lesions was evaluated by Gensini scoring method and the association between severity of coronary artery lesions and serum hs-CRP levels and other risk factors were examined.

**Results.** No significant difference was found between the two groups in terms of gender. Severity of lesions had no significant difference according to Gensini score in women compared with men. Mean Gensini score was significant between the two groups ( $66.79 \pm 48.12$  in hs-CRP positive group versus  $21.09 \pm 26.25$  in negative ones,  $p < 0.05$ ). In addition, diabetic patients were significantly more in hs-CRP positive group than negative hs-CRP group ( $P < 0.05$ ). In terms of smoking, there was a significant difference between the two groups. Percentage of patients with hypercholesterolemia was significantly higher in hs-CRP negative group. There was a significant difference in severity of lesions between smokers and non-smokers.

**Conclusion.** No significant correlation was observed between serum levels of hs-CRP and severity and angiographic extent on coronary arteries in our study. Considering the potential risk of coronary inflammatory process as a new variable, it can help discover new cases of coronary lesions and follow-up and control of the selected cases.

**Keywords:** coronary artery disease, hsC-reactive protein, inflammation

### Background

Despite important advances in the diagnosis and treatment of coronary artery disease, it is still among the most common causes of death and disability in the world, which endangers global health. Coronary artery disease

(CAD) is the principal cause of disability and mortality worldwide, and its prevalence is increasing around the world [1]. Knowing the risk factors for coronary disease such as hypertension, diabetes, insulin resistance, dyslipidemia, positive family history, smoking, limited movement, obesity, psychological stress, and recently homocysteine and inflammatory markers are of great importance [2,3]. Factors such as age, diabetes, lipid profile, smoking, gender and heredity are introduced as risk factors for coronary

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artery disease [4,5]. In recent decades, the inflammatory idea of atherosclerosis has been strongly suggested and hence the measurement of inflammatory markers' levels to determine the risk of cardiovascular events in patients with stable and unstable angina [6-15].

One of these markers is hs-CRP (C-reactive protein) that has been indicated to increase in patients with coronary artery atherosclerosis and is associated with disease severity and its complications [16].

Habib and Masri have concluded that patients with angiographically evaluated coronary artery disease have significantly higher levels of hs-CRP levels compared to healthy individuals and are associated with the severity and presence of CAD [17].

Guruprasad and colleagues have suggested that higher levels of hs-CRP are independently associated with increased risk of coronary artery disease [18].

Younan and Al-Khashab have suggested that the serum level of hs-CRP is associated with presence, but not the severity of CAD in patients with chronic stable angina [19]. Many studies have shown that small amount of increased hs-CRP is a good predictor for disease and its complications, because of its high sensitivity [4-16]. Underlying mechanisms of hs-CRP as a catalyst or intensifier of acute coronary syndrome, like MI, is not exactly known. Some researchers have shown that hs-CRP probably activate complement and cause continuing of the inflammation process of atheromatous plaques or create rupture or bleeding in the plaque, and whether hs-CRP level is correlated with the severity of the injury remains unknown [20]. Various studies have indicated hs-CRP as a predictor of cardiovascular events such as myocardial infarction, stroke, peripheral vascular obstruction among apparently healthy men and women as well as the elderly and smokers [21-23]. Rashidinejad and colleagues concluded that high-sensitivity CRP level is a clinical parameter that was not associated with the severity of coronary artery disease [24]. Several investigations in healthy as well as high-risk individuals have demonstrated a relationship between CRP and the risk of coronary artery disease (CAD) [25,26]. In addition, hs-CRP may be a sensitive predictor of future cardiovascular events in healthy individuals [27]. Koc and colleagues have investigated the variation of hs-CRP levels and their association with the severity of CAD in patients with stable CAD. They measured temporal hs-CRP levels in 124 patients (94 with CAD, 30 with normal coronary arteries), who were evaluated via coronary angiography and Gensini scoring [28]. Ridker has reported that high-sensitivity CRP is a very good predictor of vascular events in the studied population and hs-CRP provides prognostic information beyond low-density lipids (LDL). Ridker has showed that at all levels of LDL and at all levels of metabolic syndrome, CRP provides additive information on vascular risk [29]. A comprehensive review of current knowledge regarding cardiovascular risk and hs-CRP have provided by Silva and Lacerda with

an analysis of the role of hs-CRP in cardiovascular risk evaluation [30]. Moreover, diabetes requires persistent medical care to prevent cardiovascular complications [31]. Roghani Dehkordi concluded that hs-CRP is strongly associated with CAD in diabetic patients [32]. Overall, there is limited and controversial data regarding changes in hs-CRP level in patients who have coronary artery disease [33].

High sensitivity CRP is reported to exist in very small amounts in serum and fluids of healthy subjects (normal value in the serum: about 3.5 mg per liter), but in inflammatory reactions, amounts of hs-CRP suddenly rise up to 3,000 times its normal amount within 6 to 48 hours. Serum levels of hs-CRP also increase in diseases such as bacterial infections, viral infections, rheumatic fever, acute myocardial infarction, cancers, rheumatoid arthritis, and tuberculosis. Amount of hs-CRP also increases after surgery, transferring large amounts of blood, vaccinations, and pulmonary embolism. In myocardial infarction, measuring hs-CRP test can be the best and most sensitive laboratory test that can predict signs of necrosis or inflammation of the heart muscle tissue. High sensitivity-CRP could cause bacterial opsonization.

Applications for diagnosis or measurement of hs-CRP in serum:

1. Proving the existence of hs-CRP in serum is diagnostic for diseases such as infections, cancers, inflammatory diseases, especially heart attacks.
2. Measurement of serum hs-CRP or its serum titration can show the extent of disease.
3. Measurement of hs-CRP at different time intervals can control the disease treatment procedure, and effectiveness of the treatment.

Although the majority of studies suggest the close relationship between the atherosclerotic diseases and increased serum levels of hs-CRP, some studies have considered measurement of the serum hs-CRP less important.

Given the importance of coronary artery disease as the leading cause of death in today's world, finding new methods and replacing early diagnostic facilities instead of treatment facilities and prevention of morbidity and mortality is very important. Therefore, with regard to uncertainties, we decided to assess the role of hs-CRP in coronary artery disease and the relationship between serum hs-CRP levels with the severity of coronary artery lesions.

The main objective of this study was to determine the relationship between serum levels of hs-CRP and coronary lesion severity. Secondary objectives included (1) Determination of serum hs-CRP levels according to gender, presence of diabetes, hypertension, lipid profile, and smoking, (2) Determination of the severity of coronary lesions according to gender, presence of diabetes, hypertension, lipid profile, and smoking, (3) Determination of the relationship between serum levels of hs-CRP and coronary lesion severity.

**Methods**

In this cross-sectional study, 102 patients referred to the angiography ward of Imam Khomeini hospital from January to March 2007 who underwent consequent blood samples to measure serum levels of hs-CRP that were sent to the laboratory of Imam Khomeini Hospital.

Blood samples were taken from patients who referred for coronary angiography and had eligible inclusion criteria and no exclusion criteria to measure serum levels of hs-CRP.

**Data collection method:** Data about age, gender, diabetes, hypertension, hyperlipidemia, or smoking was collected from the information system of the angiography ward. Patients underwent coronary angiography and the severity of coronary lesions was assessed by two professors by Gensini scoring method. Inclusion criteria for recruiting patients into the study included any coronary patient with stable angina. Exclusion criteria of the study were the circumstances that led to the withdrawal of patients from the study, including the following:

1. Any infectious disease during the last 48 hours
2. Rheumatic diseases, such as vascular collagen diseases
3. Malignancies
4. Infection on catheter site
5. Urinary tract infections
6. Recent surgery
7. History of receiving high amounts of blood

**The sample size calculation method and number**

Regarding the relationship between hs-CRP and the number of segments involved with  $r=0.3$  [34], a sample size of 102 was calculated according to the following formula:

$$n = \frac{Z_{\alpha} - Z_{\beta}}{C}, C = 0.5 \times Ln \left( \frac{(1+r)}{(1-r)} \right)$$

$\alpha=0.05, \beta=0.1, r=0.3$

Received samples were centrifuged in the laboratory and serum hs-CRP levels were measured by Latex-high sensitivity method by Biosystem kit made in Spain. Level higher than  $7.9 \mu\text{g/ml}$  was considered as positive serum hs-CRP (case). Normal range of CRP is  $5$  to  $8 \mu\text{g/ml}$  and minimum detectable amount with the kit is  $1 \mu\text{g/ml}$ . Then the patients underwent coronary angiography and the numbers of involved coronary arteries were measured and the severity of coronary lesions was assessed by two professors by Gensini scoring method.

Information on age, gender, diabetes, hypertension, hyperlipidemia, and smoking was derived from angiography ward information system. Patients who had a history of taking anti-hypertensive during the last six months or had a blood pressure higher than  $140.9 \text{ mmHg}$ , were regarded as hypertensive. Patients with a history of taking anti-diabetic drugs or had an  $\text{FBS} > 126 \text{ mg/dl}$  or  $\text{BS} > 200 \text{ mg/dl}$  were included in diabetic patients group. Patients

were considered smokers when they had smoked during the previous month. As defined, patients were included in hyperlipidemic patients when their blood cholesterol was higher than  $200 \text{ mg dl}$  or had a history of taking anti-lipidemic drugs.

Angiography was performed for patients using the Judkins method. Stenosis of coronary arteries was defined as significant when about 50% of the normal diameter of the vessel in one or more main coronary vessels (LAD, LCX, and RCA) had stenosis. Patients with more than 50% left main coronary involvement were considered as double-vessel patients.

Data from the measurement of serum levels of hs-CRP with angiographic information and risk factors were logged in the checklist, previously designed for this purpose, and results were analyzed by SPSS software and analyzed by Pearson correlation test, t-test, and Chi test.

**Results**

**Demographic data of patients in the two groups**

A total of 102 patients participated in the study, 63 men (61.8%) and 39 women (38.2%) (Figure 1). In patients with positive hs-CRP, 12 patients were male (57.1%) and 9 female (42.9%). In patients with negative hs-CRP, 51 patients were male (63%) and 30 female (37%). No statistically significant difference existed between the two groups in terms of gender (Table I).

Mean age of patients was  $60.16 \pm 9.13$  years, ranging from 39 to 77 years. In positive hs-CRP group, mean age of patients fluctuated between 54 to 77 years. In negative hs-CRP group, the mean age was  $59.25 \pm 9.36$  years (Figure 2). Although patients with positive hs-CRP had a higher mean age than patients with negative hs-CRP, no significant relationship was observed between the two groups in terms of age. In the case group, also, no significant correlation was observed between the mean age of this group between men and women (Table II).

**Comparing the severity of coronary lesions by Gensini score**

Gensini score was variable in all patients from 0 to 178 and had a mean of  $30.5 \pm 36.73$ . In positive hs-CRP group, mean Gensini score amount was  $66.79 \pm 48.12$  and its amount varied from 11 to 178. In negative CRP group, mean Gensini score was  $21.09 \pm 26.25$  and the changes ranged between 0 and 92 in this group. Statistically significant difference was observed between the two groups ( $P < 0.05$ ). Mean Gensini score in men and women with positive hs-CRP did not show statistically significant difference (Table III).

**Assessing mean hs-CRP between the two groups**

Statistical analysis showed that the mean serum level of hs-CRP in the total group was  $5.16 \pm 6.31$  (range of 0.1 to 37.25), mean in the positive hs-CRP group was  $15.07 \pm 7.35$  (ranging between 8.6 and 37.25) and in the negative hs-CRP group was  $2.60 \pm 2.11$  (ranging between

0.1 and 7.80). Statistically significant difference was observed between the mean hs-CRP between the two groups ( $P < 0.05$ ) (Figure 3). Comparison of hs-CRP serum levels in male and females in positive hs-CRP group did not show a significant relationship (Table IV).

#### **Evaluation of risk factors between the two groups**

Generally, the percentage of patients with diabetes was reported 26.5% ( $n=27$ ). Statistics of diabetes was 71.4% ( $n=15$ ) in positive hs-CRP group and 14.8% ( $n=12$ ) in negative hs-CRP group that showed a significant difference between the two groups in terms of diabetes ( $p < 0.05$ ) (Figure 4, Table V). There was also no difference between the two groups in terms of diabetes (Table VI).

Regarding hypertension, in the whole group, the percentage of patients with hypertension was reported 32.4% ( $n=33$ ). Statistics of hypertension in the positive hs-CRP group was 47.6% ( $n=23$ ) and in the negative hs-CRP group was 28.4% ( $n=10$ ), which had no significant difference between the two groups regarding hypertension ( $P=0.09$ ) (Figure 5, Table VII). The statistical analysis showed no significant association between men and women in the group with positive hs-CRP (Table VIII).

Smokers included 25.5% ( $n=26$ ) of patients, 14.8% ( $n=12$ ) of which were in hs-CRP negative group and 66.7% ( $n=14$ ) in positive hs-CRP group. Statistical analysis showed that smoking was not significantly different between the two groups ( $P=0.09$ ) (Figure 6, Table IX). There was a significant association between men and women in terms of smoking in positive hs-CRP group (Table X).

Generally, the percentage of patients with hypercholesterolemia was reported 37.3% ( $n=38$ ). Statistics of having hypercholesterolemia in positive hs-CRP group was 66.7% ( $n=14$ ) and in negative hs-CRP group 29.6% ( $n=24$ ), which showed a significant difference between the two groups in terms of development of hypercholesterolemia. This means that the percentage of patients with hypercholesterolemia was significantly higher in negative hs-CRP group ( $P=0.02$ ) (Figure 7, Table XI). Statistical analysis showed no significant relationship between men and women in the group with positive hs-CRP (Table XII).

#### **The severity of coronary lesions and its relationship with gender**

Statistical analysis showed that the severity of lesions by Gensini score had no significant differences in women compared with men. Mean Gensini score was

$32.69 \pm 42.44$  in women and  $29.13 \pm 33.00$  in men (Table XIII). Also, there was no significant relationship in the severity of lesions between men and women in the group with positive hs-CRP (Table XIV).

#### **The severity of coronary lesions and its relationship with hypertension**

Statistical analysis showed that the severity of lesions according to Gensini score had no significant difference in hypertensive group compared to the group with normal blood pressure. Mean Gensini score in hypertensive patients, was  $44.17 \pm 32.56$  and in the group with normal blood pressure was  $23.96 \pm 37.03$  (Table XV).

#### **The severity of coronary lesions and its relationship with smoking**

Mean Gensini score was  $45.29 \pm 8.88$  in smokers and  $29.88 \pm 3.42$  in non-smokers. Statistical analysis showed a significant difference in the severity of lesions according to Gensini score between smokers and non-smokers (Table XVI).

#### **The severity of coronary lesion and its relationship with hypercholesterolemia**

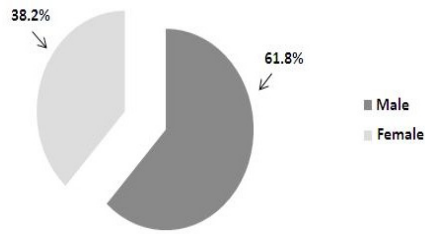
Statistical analysis showed no significant difference in the severity of lesions according to Gensini score in patients with hypercholesterolemia compared with patients with normal serum cholesterol. Mean Gensini score in patients with hypercholesterolemia was  $35.71 \pm 38.43$  and in patients with normal serum cholesterol was  $24.07 \pm 35.63$  (Table XVII).

#### **The severity of coronary lesions and its relationship with diabetes**

Mean Gensini score was  $36.50 \pm 25.75$  in patients with diabetes and  $28.33 \pm 39.88$  in the group without diabetes (Table XVIII). Statistically, the severity of lesions, according to Gensini score, was not significantly different in diabetic patients compared with non-diabetic patients.

In the next step, we compared the severity of coronary artery lesions between men and women in positive hs-CRP group with Pearson correlation test. Statistically, the studied women and men had no significant difference regarding the severity of coronary lesions (Table XIX).

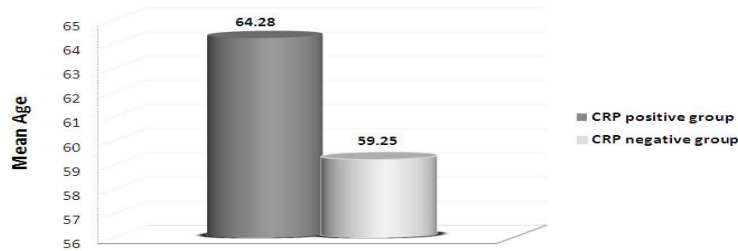
Statistical studies by Pearson correlation test on men and women represented no significant difference between the number of involved vessels (confirmed by angiography) and patients' gender (Table XX). The severity of coronary artery lesions and hs-CRP levels are compared as shown in Figure 8.



**Figure 1.** Frequency of patients participating in the study.

**Table I.** Frequency of patients participating in the study according to gender.

	Hs-CRP positive group	Hs-CRP negative group	P value
Women patients	42.9%	37%	0.6
Men patients	57.1%	63%	



**Figure 2.** Mean age of the CRP positive and negative groups.

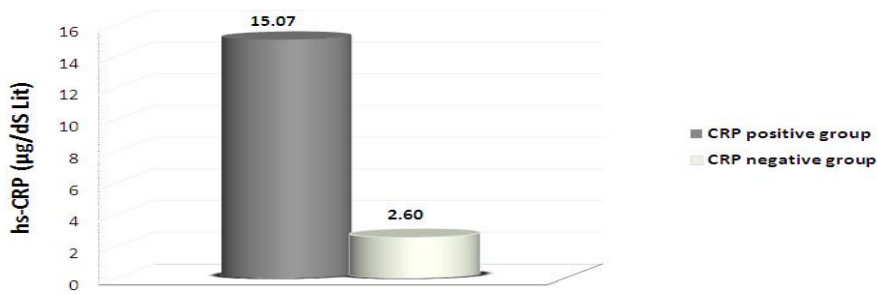
**Table II.** Comparing the mean age of men and women in study group.

Hs-CRP positive group	Mean age	P value
Women	62.48±2.34	0.7
Men	63.24±1.49	

**Table III.** Mean Gensini score in men and women with positive CRP.

Hs-CRP positive group	Gensini score	P value
Women	85.67±16.34	0.1
Men	52.63±12.75	

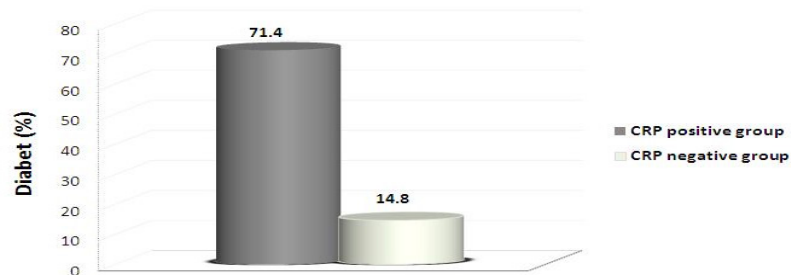




**Figure 3.** The mean serum levels of hs-CRP.

**Table IV.** The mean serum levels of hs-CRP in men and women with positive hs-CRP.

Hs-CRP positive group	Mean serum levels of hs-CRP	P value
Women	15.58±9.79	0.7
Men	14.68±5.31	



**Figure 4.** Comparing the diabetic patients.

**Table V.** Comparing the diabetic patients in hs-CRP positive and negative groups.

	N	% of the total	In diabetic patients	P value
Hs-CRP positive group	15	71.4	55.6%	<0.05
Hs-CRP negative group	12	14.8	44.4%	

**Table VI.** Comparing the diabetic patients in women and men in positive hs-CRP group.

Hs-CRP positive group	N	% of the total	In hs-CRP positive group	P value
Women	5	55.6%	33.3%	0.1
Men	10	83.3%	66.7%	

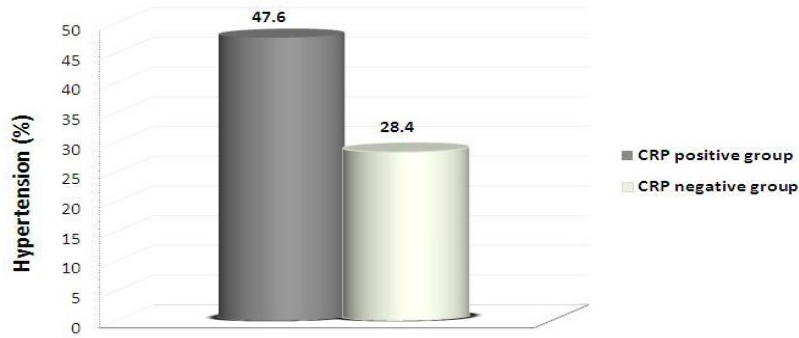


Figure 5. Comparing patients with hypertension.

Table VII. Comparing patients with hypertension in hs-CRP positive and negative groups.

	N	% of the total	In HTN patients	P value
Hs-CRP positive group	23	47.6%	69.7%	0.09
Hs-CRP negative group	10	28.4%	30.3%	

Table VIII. Comparing patients with hypertension in women and men in positive CRP group.

Hs-CRP positive group	N	% of the total	In hs-CRP positive group	P value
Women	3	33.3%	30%	0.2
Men	7	58.3%	70%	

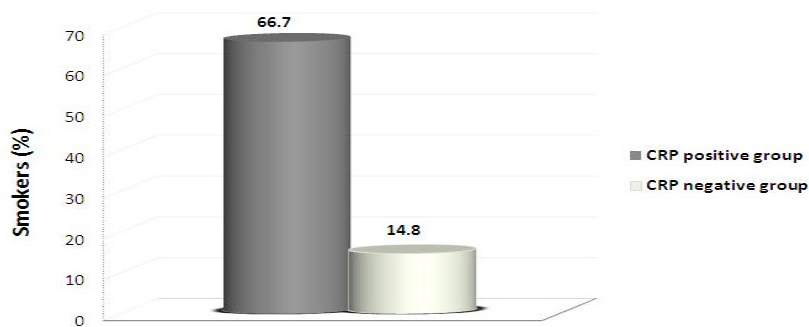


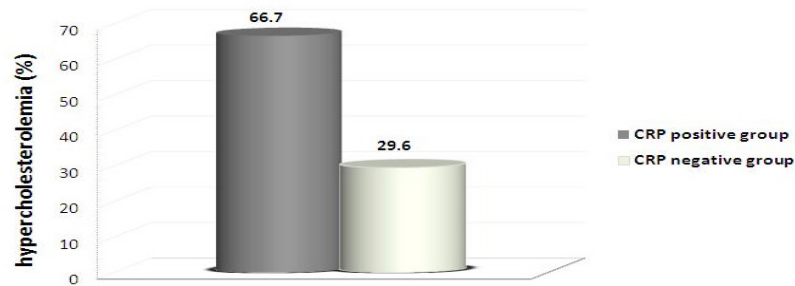
Figure 6. Comparing the percentage of smokers.

Table IX. Comparing the percentage of smokers in hs-CRP positive and negative groups.

	N	% of the total	In smoker patients	P value
Hs-CRP positive group	14	66.7%	53.8%	0.09
Hs-CRP negative group	12	14.8%	46.2%	

**Table X.** Comparing the percentage of men and women smokers in positive CRP group.

Hs-CRP positive group	N	% of the total	In hs-CRP positive group	P
Women	2	22.2%	85.7%	<0.05
Men	12	100%	14.3%	

**Figure 7.** Comparing patients with hypercholesterolemia.**Table XI.** Comparing patients with hypercholesterolemia in hs-CRP positive and negative groups.

	N	% of the total	In hypercholesterolemia patients	P value
Hs-CRP positive group	14	66.7%	36.8%	0.02
Hs-CRP negative group	24	29.6%	63.2%	

**Table XII.** Comparing patients with hypercholesterolemia in women and men in positive hs-CRP group.

Hs-CRP positive group	N	% of the total	In hs-CRP positive group	P value
Women	4	44.4%	33.3%	0.3
Men	8	66.7%	66.7%	

**Table XIII.** Comparing the severity of coronary lesions in men and women patients.

	N	Gensini score (Mean± SD)	P value
Women Patients	39	32.69±42.44	0.6
Men Patients	63	29.13 ± 33.00	

**Table XIV.** Comparing the severity of coronary lesions between men and women in the group with positive hs-CRP.

	N	Gensini score (Mean±SD)	P value
Women Patients	9	85.67±16.34	0.1
Men Patients	12	52.63±12.75	



**Table XV.** Comparing the severity of coronary artery lesions in hypertensive and non-hypertensive patients.

	N	Gensini score (Mean± SD)	P value
Hypertensive Patients	33	44.17±32.56	0.09
Non-hypertensive Patients	69	23.96±37.03	

**Table XVI.** Comparing the severity of coronary artery lesions in smokers and non-smokers patients.

	N	Gensini score (Mean± SD)	P value
Smoker Patients	26	45.29±8.88	0.01
Non-smoker Patients	76	29.88±3.42	

**Table XVII.** Comparing the severity of coronary artery lesions in patients with hypercholesterolemia and patients with normal serum cholesterol.

	N	Gensini score (Mean±SD)	P value
Hypercholesterolemia Patients	38	35.71±38.43	0.2
Non-hypercholesterolemia Patients	64	24.07±35.63	

**Table XVIII.** Comparing the severity of coronary artery lesions in diabetic and non-diabetic patients.

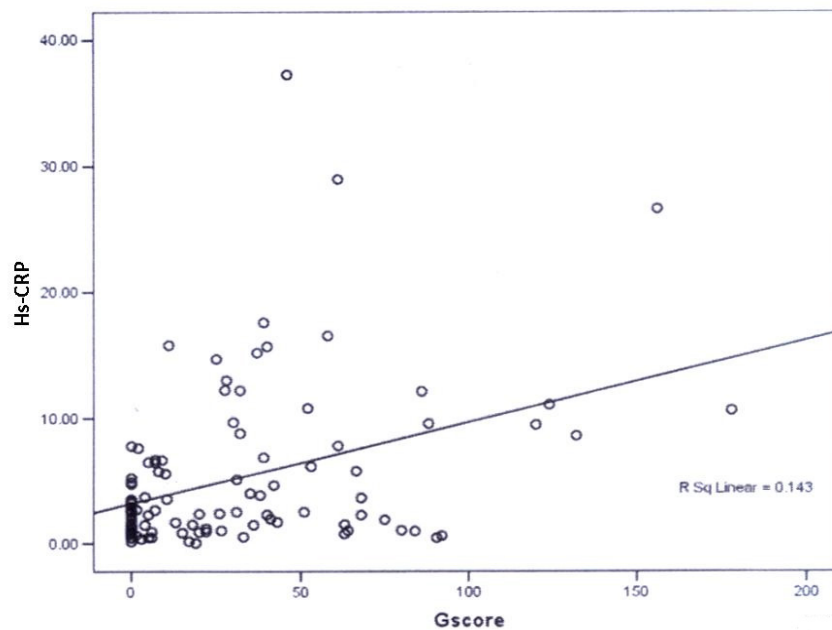
	N	Gensini score (Mean±SD)	P value
Diabetic Patients	27	36.50±25.75	0.3
Non- diabetic Patients	75	28.33±39.88	

**Table XIX.** Assessing the relationship between hs-CRP and coronary lesion severity with Pearson correlation coefficient between men and women in the whole group.

	Number	P value	r
Women	39	0.24	0.19
Men	63	0.24	0.15
Total	102	0.13	0.15

**Table XX.** Comparing the relationship between sex hs-CRP and coronary lesion severity by Pearson correlation.

	Number	Mean involved vessels	P value
Women	39	0.19	0.24
Men	63	0.15	



**Figure 8.** Comparing the severity of coronary artery lesions and hs-CRP levels.

## Discussion

In summary, the objective of this study was to identify the hs-CRP as a definite inflammation marker in estimating coronary lesions in patients with stable angina after the initial symptoms. Although the studied population was limited to patients with stable angina, we estimate that hs-CRP levels also rise significantly in unstable angina and MI [35]. The proof of our claim for increased hs-CRP in patients with stable angina is the previous studies that confirm our results [36-37].

Berk and Liuzzo have found that serum levels of hs-CRP increased in both groups of patients with stable angina and unstable angina and this marker is considered as a reliable indicator to predicting future events in these patients [36-37]. But these researchers have found that hs-CRP could not clinically differentiate between patients with stable angina and acute coronary syndrome patients. These studies also found that about 13% of patients with stable angina had increased serum hs-CRP levels in the absence of clinical symptoms that is probably due to this effect that the number of activated macrophages that succeed to reach the plaque site are very few because of small size of the involved coronary vessels. Thus, the increased level of hs-CRP is much less than the amount to be detected by laboratory methods.

Results of our study may indicate the importance of hs-CRP determination for evaluation of coronary artery lesions in the Iranian population. Although uncertainty exists in some studies to measure hs-CRP as an agent to estimate coronary lesions, other case-control and cross-sectional studies show the strong association between these

two variables [38-39].

A meta-analysis that merged the results of seven major studies, clearly indicated that even after the correction of a number of important factors in heart disease, hs-CRP remained a risk factor in the final analysis [40].

On the other hand, confounding factors are also available which may affect the priority of serum hs-CRP levels in patients with stable angina and even with extensive coronary lesions. One of these factors is aspirin administration that exists in most treatment protocols for these patients. Another drug is statins with proven anti-inflammatory properties.

Studies have shown that eliminating patients taking aspirin and statins have considerably increased hs-CRP possibility and its association with coronary lesion severity in re-analysis [41, 42].

Azar and colleagues [43] have concluded in their study on 98 patients with CAD that there is no correlation between serum hs-CRP and the severity of coronary lesions and the number of involved vessels (confirmed by angiography), although 20% of the patients had a history of myocardial infarction and history of PCI in more than two weeks ago. Another published study also confirmed results of the previous studies. In this study, there were patients who were taking statins and 62% of patients had a history of MI in the last two years [44].

Other studies concluded that hypercholesterolemia (ratio of total cholesterol to HDL) is also directly correlated with serum hs-CRP levels. A ratio of HDL to cholesterol above 5 is considered as increased hs-CRP and increased risk for the occurrence of myocardial infarction in the

future [45-46].

Generally, the obtained result indicates that the effect of risk factors for CAD (such as high hs-CRP and lipid profile) have cumulative effect on the incidence of coronary diseases. The above-mentioned studies confirm the current study, in which significant relationship was observed between serum levels of hs-CRP in patients with hypercholesterolemia and patients with normal levels of serum cholesterol.

Ford and colleagues conducted a study to examine the association between risk factors for cardiovascular diseases and found a significant relationship between serum levels of hs-CRP and other risk factors such as age, BMI, and serum total cholesterol level [47]. Another study also confirmed similar relationship between serum hs-CRP levels, smoking, and diabetes [48].

Unlike the two previous studies, another study rejected the relationship between the classic risk factors for heart disease and serum hs-CRP [49]. This discrepancy between the results, obtained from different studies, reflect differences in the studied subjects across the world and also due to the low number of subjects in the studies. Our evaluation also showed a clear and significant difference between serum hs-CRP and diabetes, but there was no significant difference regarding smoking and hypertension.

Hs-CRP, synthesized in the liver, is mainly under the control of inflammatory cytokines and interleukin-6 [50]. In healthy people, weight gain leads to an increased amount of interleukin-6 and this phenomenon may lead to increased hs-CRP. Recently, the role of obesity and increased CRP is proven in children [51], while about one-third of IL-6 circulating in the blood originates from the adipose tissue [52]. Thus, IL-6 may facilitate increased hs-CRP levels in obese patients as a bridge. Several studies have confirmed the relationship between increased hs-CRP, obesity, and hypertension [53].

The number of coronary vessels with report of more than 50% stenosis in angiography has a direct correlation with the amount of hs-CRP. This theory has been proven by a number of studies [54,55]. However, no connection was found in a number of other studies [41-42]. In the present study, also, we did not encounter significant relationship.

Recent research indicated that approximately 50% of cardiovascular diseases happen in patients with HDL of lower than normal level [53]. In these people, a significant increase in their LDL levels has been observed. Ridker and colleagues [42] concluded that hs-CRP could be a strong factor to predict the likelihood of future events in patients with a history of myocardial infarction, stable angina, and normal levels of serum lipids.

In another prospective study, Ridker and colleagues found that the measurement of serum hs-CRP predicts the risk of future cardiovascular events in women with serum LDL levels of less than 3.4 mmolL<sup>-1</sup> [46].

## Conclusion

No significant correlation was observed between serum levels of hs-CRP and severity and angiographic extent on coronary arteries in our study. Considering the potential risk of coronary inflammatory process as a new variable, it can help discover new cases of coronary lesions and follow-up and control of the selected cases.

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