Clinical and angiographic correlation of high-sensitivity C-reactive protein with acute ST elevation myocardial infarction

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Abstract. Vascular inflammation and associated ongoing inflammatory responses are considered as the critical culprits in the pathogenesis of acute atherothrombotic events such as acute coronary syndrome (ACS) and myocardial infarction (MI). ST segment elevation myocardial infarction (STEMI) is considered as one of the prominent clinical forms of ACS. Moreover, C-reactive protein (CRP) is an important acute phase prsotein, which may be estimated using high-sensitivity methods (hs-CRP), and its elevated level in body fluids reflects chronic inflammatory status. The circulating hs-CRP level has been proposed as a promising inflammatory marker of coronary artery disease (CAD). The present study investigated the correlation of hs-CRP level with clinical and angiographic features of STEMI, various other traditional risk factors, complications of myocardial infarction and angiographically significant CAD. Out of 190 patients with STEMI that were analyzed, the interval between symptom onset and reperfusion therapy (window period) varied from 0.5 to 24 h. The hs-CRP value was found to be higher in non-diabetic patients (0.61 mg/dl) compared with diabetic patients (0.87 mg/dl). Moreover, a significant correlation between hs-CRP and hs-troponin T was also recorded (P<0.001). However, there was no significant difference in the mean hs-CRP values in patients with or without mortality. It is considered that the present study will increase the understanding of atherosclerosis in general and may also have clinical applications in the targeting of therapy for this harmful disease.

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Introduction

Over the past several years, it has become clear that inflammatory processes regulate atherosclerotic disease at a fundamental level (1). Fewer than 50% of cases of coronary artery disease (CAD) can be ascribed to traditional risk factors and the remaining cases are unexplained (2).

C-reactive protein (CRP) has emerged as the leading candidate marker for systemic inflammation, because of its predictive ability, wide availability, low cost and ease of use (3). It is a calcium-binding pentameric protein consisting of five identical, non-covalently linked, 23-kD subunits produced in the liver in response to interleukin (IL)-6, IL-1 and tumor necrosis factor. CRP levels begin to rise within 4-6 h after tissue injury and can continue to rise exponentially to increase several hundred fold within 24-48 h. Moreover, the half-life of CRP is <24 h (1,3). The predictive power of CRP for vascular risk detection is in the range of 0.1 to 0.5 mg/dl, a level found in many healthy individuals without inflammation (4). Hence, CRP assays are required to be highly sensitive High-sensitivity CRP (hs-CRP) has a limit of detection as low as 0.02 mg/dl and is a well standardized assay (5,6). Various trials have shown that the predictive value of hs-CRP is significantly higher compared with those of other traditional cardiovascular risk markers (7,8).

The purpose of the present study was to investigate the association of hs-CRP with acute ST elevation myocardial infarction (STEMI), and its correlation with various other traditional risk factors, complications of myocardial infarction (MI) and angiographically significant CAD.

Materials and methods

Patients. The study included 190 consecutive patients with a diagnosis of acute STEMI admitted to the Coronary Care Unit (CCU) at Sri Jayadeva Institute of Cardiovascular Sciences and Research (Bangalore, India). The cross-sectional study was carried out between December 2012 and April 2013. The study was conducted in accordance with the Declaration of Helsinki and with approval from the ethics committee of Sri Jayadeva Institute of Cardiovascular Sciences and Research. Informed consent was obtained from all individual participants.

The diagnosis of acute MI was made on the basis of the Joint ESC/ACCF/AHA/WHF Task Force's Third Universal Definition (9). Patients with diabetes mellitus had a fasting plasma glucose concentration >126 mg/dl, glycated hemoglobin level >6.5%, or were receiving treatment with insulin or hypoglycemic agents. Patients who had a systolic/diastolic blood pressure >140/90 mmHg or were currently using any antihypertensive medication were defined as hypertensive. Cigarette smoking was defined as active smoking in the last 6 months. Patients diagnosed with unstable angina and NSTEMI, were excluded from the study. According to a previously designed questionnaire, data included gender, age, body mass index (BMI), blood pressure and assessment of risk factors, including a history of MI. During baseline evaluation, symptoms were assessed, Killip class was assessed, and a thrombosis in MI (TIMI) score was calculated for all patients (10). Blood samples were drawn from patients at the time of admission to the CCU for the analysis of random blood glucose (RBS), renal function, serum electrolytes, lipid parameters, complete blood count, high-sensitivity (hs)-troponin T and hs-CRP. An echocardiographic evaluation of the left ventricular ejection fraction (LVEF) was performed in all participants within 24 h of hospital admission. Blood samples were processed within 24 h using automated micro-particle immunoassays (ELISA Immuno Explorer Kit; Bio-Rad Laboratories, Inc., Hercules, CA, USA). The hs-CRP detection range was 0.1-12.0 mg/dl, with an inter-assay variation coefficient of <5%.

Angiographic assessment of coronary atherosclerosis. Two experienced cardiologists with no prior knowledge of the patients' biochemical results reviewed all angiographic images to assess the extent of CAD and morphology of all coronary artery stenosis. A significant CAD was defined based on the presence of >50% coronary artery stenosis in any coronary artery or left main artery. A Syntax score was calculated for all coronary angiograms (CAGs) using on an online Syntax score evaluating algorithm version 2.1 (www.syntaxscore.com). Patients were divided into three groups on the basis of Syntax score: Low Syntax score (0-22 points), intermediate Syntax score (23-31 points) and high Syntax score (≥33 points), and mean hs-CRP values were compared among these three groups (11).

Statistical analysis. All statistical analyses were performed using SPSS version 16.0 software (SPSS Inc., Chicago, IL, USA). Baseline characteristics were assessed with the Student's t-test (parametric) and Mann-Whitney U test (non-parametric) for continuous variables, and the χ^2 test for categorical variables, with two-tailed P-values. P<0.05 was considered to indicate a statistically significant difference.

Results

Baseline characteristics. Baseline characteristics of the study population comprising 190 patients with STEMI were analyzed. The patient age ranged from 20 to 90 years (mean, 54.37 years), as shown in Table I. Among those 190 patients, 150 (79%) were males and 40 (21%) were females. Anterior wall myocardial infarction (AWMI) was found to be the most common type of MI, present in 94 patients (49.5%). Lateral wall MI (LWMI) was found to be the least common type, present in only 0.5% of patients (Table II). The interval between symptom onset and reperfusion therapy (window period) varied from 0.5 to 24 h, with a mean value of 5.59 h (Table I). Coronary risk factor frequencies such as hypertension were present in 37%, type 2 diabetes mellitus in 38% and dyslipidemia in 83% of patients (Table II). Patients with hs-CRP ≥0.5 mg/dl had a higher mean age (P=0.029).

hs-CRP and various risk factors. There was no correlation between hs-CRP and various lipid parameters, serum creatinine, RBS, white blood cell count and platelet count (Table III). However, the mean values of hs-CRP were found to be higher in patients with hypertension, smoking and high total cholesterol (Table II). A significant difference in hs-CRP values was recorded between patients with diabetes and those without diabetes (P=0.029). RBS also had a positive correlation with hs-CRP values (r=0.165, P=0.023; Table III); however, no statistically significant difference in the mean value of hs-CRP was recorded between patients with normal and abnormal RBS. With regards to total cholesterol, mean hs-CRP values were found to be higher in patients with total cholesterol levels >200 mg/dl (mean hs-CRP values 0.66 vs. 0.76 mg/dl; P=0.068; Table II). A significant correlation between hs-CRP and hs-troponin T (r=0.306, P<0.001; Table III) was also recorded.

hs-CRP and clinical factors. A significant difference was observed in the mean hs-CRP values with regard to duration of the window period (Table I). Out of 190 patients, 141 patients were found to have a window period between 0 and 6 h; among them 77 patients had hs-CRP levels <0.5 mg/dl and 64 patients had hs-CRP levels ≥0.5 mg/dl. Moreover, 49 patients presented with a window period of >6 h, with 18 patients having hs-CRP values <0.5 mg/dl, and 31 patients having hs-CRP values ≥0.5 mg/dl (P=0.05).

Table II shows that among the different types of MI, there was no statistically significant difference in the mean hs-CRP values. However, patients presenting with combined AWMI and IWMI had the highest hs-CRP values, whereas patients with IWMI had lowest hs-CRP values (1.29 vs. 0.54 mg/dl). Over all, ~50% of STEMI patients had hs-CRP elevation (>0.5 mg/dl) and the remaining 50% of patients had hs-CRP levels within normal limits (<0.5 mg/dl). With regard to left ventricular ejection fraction (LVEF), no statistically significant difference in hs-CRP values was recorded among patients with different LVEF percentages; however patients with an LVEF <30% had a higher mean hs-CRP value (0.76 mg/dl) compared with patients with an LVEF >50% (0.48 mg/dl). There was no significant correlation between hs-CRP and TIMI score (Table III), although higher TIMI scores were associated with higher hs-CRP values. There was a significant difference in hs-CRP values among patients with different Killip classes (P<0.029), with higher mean hs-CRP values observed in patients with higher Killip classes (Table II).

hs-CRP and coronary angiography. Following coronary angiography, single, double and triple vessel CAD was identified in 43, 25 and 7 patients, respectively (Table IV). Tables IV-VI show the associations between hs-CRP and CAG findings.

Table I. Patient data and window period.

Parameter	Mean	SD	SE of mean	Median	Min	Max
Age (years)	54.37	11.73	0.85	55	20	90
Weight (kg)	59.66	8.55	0.62	58	45	92
Height (cm)	155.25	4.35	0.32	155	148	165
BMI (kg/m^2)	24.67	2.69	0.20	24.44	19.98	35.94
Window period (h)	5.59	3.70	0.27	5	0.50	24

BMI, body mass index; SD, standard deviation; SE, standard error.

Table II. Patient clinical parameters.

					95% CI for mean				
Parameter	N	Mean hs-CRP (mg/dl)	SD	SE of mean	Lower bound	Upper bound	Min	Max	P-value
MI type									0.279
AWMI	94	0.67	0.82	0.08	0.51	0.84	0.02	4.67	
AWMI + LWMI	4	0.98	1.22	0.61	-0.97	2.92	0.06	2.77	
IWMI	26	0.54	0.48	0.09	0.35	0.74	0.01	1.50	
IWMI + RVMI + PWMI	13	0.65	0.53	0.15	0.33	0.97	0.05	1.60	
IWMI + PWMI	26	0.92	0.94	0.18	0.54	1.30	0.06	4.98	
IWMI + RWMI	22	0.73	0.79	0.17	0.38	1.08	0.02	3.34	
AWMI + IWMI	3	1.29	1.14	0.66	-1.54	4.11	0.30	2.53	
LWMI	1	0.85	-	-	-	-	0.85	0.85	
Hypertension									0.181
Absent	120	0.69	0.87	0.08	0.54	0.85	0.01	4.98	
Present	70	0.73	0.64	0.08	0.58	0.88	0.02	3.34	
Diabetes mellitus									0.029
Absent	118	0.61	0.71	0.07	0.48	0.74	0.01	4.98	
Present	72	0.87	0.88	0.10	0.66	1.07	0.02	4.51	
Smoking									0.818
Absent	87	0.69	0.77	0.08	0.53	0.86	0.02	4.51	
Present	103	0.72	0.81	0.08	0.56	0.88	0.01	4.98	
Dyslipidemia									0.419
Absent	32	0.87	0.90	0.16	0.54	1.19	0.02	3.34	
Present	158	0.67	0.76	0.06	0.55	0.80	0.01	4.98	
LVEF (%)									0.453
<30	2	0.76	0.37	0.26	-2.54	4.06	0.50	1.02	
30-40	51	0.81	0.90	0.13	0.55	1.06	0.01	4.51	
41-50	112	0.71	0.80	0.08	0.56	0.86	0.02	4.98	
>50	25	0.48	0.44	0.09	0.30	0.66	0.02	1.50	
Killip class									0.029
Class I	141	0.62	0.71	0.06	0.50	0.74	0.01	4.98	
Class II	33	0.95	1.02	0.18	0.58	1.31	0.05	4.51	
Class III	4	1.08	1.22	0.61	-0.86	3.01	0.31	2.89	
Class IV	12	0.98	0.63	0.18	0.59	1.38	0.22	2.26	
Total cholesterol									0.068
Normal	103	0.66	0.79	0.08	0.51	0.81	0.01	4.67	
Increased/risk	87	0.76	0.79	0.09	0.59	0.93	0.02	4.98	

Table II. Continued.

Parameter	N	Mean hs-CRP (mg/dl)	SD	SE of mean	95% CI for mean		Min	Max	P-value
					Lower bound	Upper bound			
HDL									0.534
Risk	118	0.68	0.82	0.08	0.53	0.83	0.01	4.98	
Normal	72	0.75	0.74	0.09	0.58	0.92	0.02	3.34	
Non-HDL									0.927
Normal	59	0.68	0.77	0.10	0.48	0.88	0.01	4.67	
Risk	131	0.72	0.80	0.07	0.58	0.86	0.02	4.98	
LDL									0.202
Normal	60	0.57	0.56	0.07	0.42	0.71	0.01	2.89	
Risk	130	0.77	0.87	0.08	0.62	0.92	0.02	4.98	
TGL									0.022
Normal	83	0.88	0.95	0.10	0.67	1.09	0.02	4.98	
Risk	107	0.57	0.61	0.06	0.46	0.69	0.01	4.51	
Hemoglobin									0.617
Anemic	47	0.72	0.73	0.11	0.51	0.94	0.02	3.34	
Normal	143	0.70	0.81	0.07	0.57	0.84	0.01	4.98	
Total WBC count									0.386
Normal	111	0.70	0.83	0.08	0.54	0.85	0.01	4.98	
Abnormal	79	0.72	0.73	0.08	0.56	0.89	0.02	4.51	
Platelet count									0.649
Normal	186	0.71	0.80	0.06	0.60	0.83	0.01	4.98	
Abnormal	4	0.49	0.54	0.27	-0.37	1.36	0.14	1.30	
RBS									0.159
Normal	80	0.66	0.83	0.09	0.47	0.84	0.01	4.98	
Abnormal	110	0.74	0.76	0.07	0.60	0.89	0.02	4.51	
Urea									
Normal	177	0.69	0.77	0.06	0.57	0.80	0.01	4.98	0.625
Abnormal	13	0.99	1.08	0.30	0.33	1.64	0.05	3.34	
Creatinine									
Normal	159	0.67	0.73	0.06	0.55	0.78	0.01	4.98	0.340
Abnormal	31	0.91	1.05	0.19	0.52	1.29	0.05	4.67	

hs-CRP, high-sensitivity C-reactive protein; SD, standard deviation; SE, standard error; CI, confidence interval; MI, myocardial infarction; AWMI, anterior wall MI; LWMI, lateral wall MI; IWMI, inferior wall MI; RVMI, right ventricular MI; PWMI, posterior wall MI; LVEF, left ventricular ejection fraction; HDL, high-density lipoprotein; LDL, low-density lipoprotein; TGL, triglycerides; WBC, white blood cell; RBS, random blood glucose.

Although there was no statistically significant difference in mean hs-CRP values among the single vessel disease (SVD), double vessel disease (DVD) and triple vessel disease (TVD) groups, hs-CRP values were higher in the DVD and TVD groups than in the SVD group (SVD, 0.56 mg/ml vs. DVD, 0.72 mg/ml and TVD, 0.97 mg/ml). Similarly there was no significant difference in mean hs-CRP values with respect to the number of vessels involved individually, but mean hs-CRP values were found to be higher in patients with a higher number of coronary arteries involved (1 vessel, 0.54 mg/ml; 2 vessels, 0.68 mg/ml; 3 vessels, 0.85 mg/ml). Moreover, there was no significant difference in the mean hs-CRP values according to Syntax scores when analyzed individually, but mean hs-CRP values correlated positively with hs-CRP value; higher hs-CRP values were observed in patients with elevated Syntax scores [Syntax score ≤22 (mild CAD), 0.59 mg/ml vs. Syntax scores >22-32 (moderate CAD), 0.89 mg/ml and >32 (severe CAD), 2.11 mg/dl; r=0.285, P=0.007; Tables III and IV]. Table VI shows the analysis of the combined study group according to hs-CRP value, where a high mean hs-CRP (≥5 mg/dl) was found to be associated with a higher number of involved coronary arteries and higher Syntax score. There was a statistically

Table III. Correlation analysis of hs-CRP and hs-TROP T.

	hs-CRP (mg/dl)		hs-Trop T (ng/ml)	
Parameter	r	P-value	r	P-value
Age	0.051	0.484	0.106	0.146
Weight	-0.030	0.681	-0.020	0.786
Height	0.018	0.805	-0.014	0.844
BMI	-0.049	0.499	-0.025	0.737
Window period	0.061	0.404	0.249	0.001
Heart rate	0.088	0.229	0.006	0.936
SBP	-0.061	0.406	-0.070	0.339
DBP	-0.073	0.314	-0.048	0.515
TIMI score	0.131	0.073	0.192	0.008
LVEF	-0.129	0.076	-0.170	0.019
Total cholesterol	0.035	0.632	0.060	0.409
HDL	0.065	0.373	0.199	0.006
Non-HDL	0.023	0.757	0.020	0.789
LDL	0.101	0.165	0.141	0.053
TGL	-0.138	0.057	-0.170	0.019
Hemoglobin	0.003	0.969	-0.003	0.969
Total WBC count	-0.013	0.858	0.069	0.341
Platelet count	-0.049	0.498	-0.136	0.061
RBS	0.165	0.023	-0.028	0.701
Urea	0.153	0.035	0.246	0.001
Creatinine	0.070	0.338	0.002	0.979
Vessel count	0.161	0.136	0.217	0.043
Syntax score	0.285	0.007	0.186	0.084
hs-CRP (mg/dl)	-	-	0.306	<0.001
hs-Trop T (ng/ml)	0.306	<0.001	-	-

hs-CRP, high-sensitivity C-reactive protein; hs-TROP T, high-sensitivity troponin T; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; TIMI, thrombosis in myocardial infarction; LVEF, left ventricular ejection fraction; HDL, high-density lipoprotein; LDL, low-density lipoprotein; TGL, triglycerides; WBC, white blood cell; RBS, random blood glucose.

significant difference in involved vessel number and Syntax score between the groups with low and high hs-CRP values (P=0.009 and P=0.019, respectively).

hs-CRP and complications. Table VII depicts the hs-CRP levels in patients with and without various in-hospital complications. No significant difference was identified in mean hs-CRP values among groups with and without various complications, with the exception of MI patients who had developed mitral regurgitation. However, the mean value of hs-CRP was found to be higher in the patients with LV dysfunction, heart failure, shock, bradyarrhythmias, tachyarrhythmias and recurrent angina than in the patients without these complications.

hs-CRP and mortality. Tables IV and VIII show that 16 patients out of 190 patients succumbed during their in-hospital stay and 1 patient succumbed at home, 20 days post discharge. There was no significant difference in mean hs-CRP values in patients with or without mortality.

Discussion

Elevated CRP has been suggested as an effective parameter for identifying the risk of future ischemic events in patients with acute coronary syndrome (ACS). Biasucci *et al* (12) reported that patients with a CRP level >0.3 mg/dl had a >8-fold higher risk of recurrent ischemic events (12).

The present study in patients with STEMI detected higher hs-CRP values (≥0.5 mg/dl) in older patients. This finding supports an earlier study which demonstrated that higher hs-CRP levels in the elderly were associated with a higher incidence of cardiovascular events compared with control subjects (13). In the present study there was a significant difference in mean hs-CRP values between patients with or without diabetes mellitus (P=0.029). A positive correlation of hs-CRP with blood sugar level was also observed (r=0.165, P=0.023). This finding is in accordance with the study by Festa *et al* (14), which showed elevated serum hs-CRP levels in metabolic disorders, namely, hypertension, dyslipidemia, type 2 diabetes and insulin resistance, suggesting the

Table IV. Association between hs-CRP and coronary angiogram data.

Parameter	N	Mean hs-CRP (mg/dl)	SD	SE of Mean	95% CI for mean		Min	Max	P-value
					Lower bound	Upper bound			
CAD									0.625
SVD	43	0.56	0.47	0.07	0.42	0.71	0.03	2.09	
DVD	25	0.72	0.71	0.14	0.43	1.01	0.01	2.77	
TVD	7	0.97	1.08	0.41	-0.03	1.97	0.08	3.34	
Insignificant CAD	12	0.76	1.28	0.37	-0.05	1.57	0.04	4.67	
No. of vessels									0.072
1	33	0.54	0.82	0.14	0.25	0.83	0.03	4.67	
2	32	0.68	0.56	0.10	0.47	0.88	0.01	2.09	
3	22	0.85	0.84	0.18	0.48	1.22	0.08	3.34	
LMCA									0.409
Unaffected	84	0.65	0.72	0.08	0.49	0.81	0.01	4.67	
Affected	3	1.20	1.38	0.79	-2.22	4.61	0.22	2.77	
Thrombus									0.979
Absent	69	0.66	0.74	0.09	0.48	0.84	0.02	4.67	
Affected	18	0.71	0.76	0.18	0.33	1.08	0.01	2.77	
Calcification									0.358
Absent	54	0.61	0.72	0.10	0.42	0.81	0.02	4.67	
Affected	33	0.76	0.78	0.14	0.48	1.04	0.01	3.34	
Syntax score									0.079
Mild CAD	75	0.59	0.65	0.07	0.44	0.73	0.01	4.67	
Moderate CAD	9	0.89	0.68	0.23	0.37	1.41	0.20	2.09	
Severe CAD	3	2.11	1.66	0.96	-2.02	6.24	0.22	3.34	
In-hospital mortality									0.171
Absent	174	0.70	0.81	0.06	0.58	0.83	0.01	4.98	
Affected	16	0.74	0.47	0.12	0.49	0.99	0.21	1.80	
30 day mortality									-
Absent	175	0.71	0.81	0.06	0.59	0.83	0.01	4.98	
Affected	1	0.31	-	-	-	-	0.31	0.31	

hs-CRP, high-sensitivity C-reactive protein; SD, standard deviation; SE, standard error; CI, confidence interval; CAD, coronary artery disease; SVD, single vessel disease; DVD, double vessel disease; TVD, triple vessel disease; LMCA, left main coronary artery.

involvement of a low-grade systemic inflammation in these disorders. In the present study, even though higher hs-CRP values were detected with the presence of hypertension, smoking, higher total cholesterol level, higher low-density lipoprotein (LDL) level, higher TIMI score and presence of LV dysfunction compared with the absence of these factors, no statistically significant difference in mean hs-CRP values was recorded. This could be due to low sample size and/or indicate the value of hs-CRP as an additive risk factor to the traditional risk factors already present as shown by earlier studies (14-17). This indicates that hs-CRP could help in the identification of patients at risk of cardiovascular events, even those previously classified as having low or intermediate risk.

Killip class in AMI is used to stratify patients with symptoms and/or signs of heart failure and predict in-hospital mortality (Killip class I has 6%, whereas Killip class IV has 60% in-hospital mortality) (18). The present study demonstrated a statistically significant difference in mean hs-CRP concentrations among patients with different Killip classes (0.62 mg/dl in Killip class I vs. 0.98 mg/ml in Killip class IV; $P<0.05$). This finding also supports an earlier study by Suleiman *et al* (19), in which it was reported that patients with acute MI had CRP levels in the upper quartile, were older, had higher baseline creatinine levels and had a greater history of heart failure.

TIMI score in AMI is a convenient, simple bedside risk scoring system for predicting 30-day mortality at presentation for fibrinolytic-eligible patients with STEMI using the In TIME-II trial database (TIMI risk score 0 has mortality 0.8%, where as TIMI score >8 has mortality 35.9%) (20). In the

Table V. Coronary angiogram findings with respect to hs-CRP value.

	hs-CRP <0.5 mg/dl		hs-CRP ≥0.5 mg/dl				
Parameter	N	%	N	%	Total	χ^2	P-value
CAD						4.143	0.216
SVD	23	53	20	47	43		
DVD	12	48	13	52	25		
TVD	1	14	6	86	7		
Insignificant CAD	7	58	5	42	12		
No. of vessels						7.065	0.029
1	22	67	11	33	33		
2	14	44	18	56	32		
3	7	32	15	68	22		
LMCA						0.322	0.570
Unaffected	42	50	42	50	84		
Affected	1	33	2	67	3		
Thrombus						0.341	0.559
Absent	33	48	36	52	69		
Affected	10	56	8	44	18		
Calcification						1.043	0.307
Absent	29	54	25	46	54		
Affected	14	42	19	58	33		
Syntax score						3.433	0.180
Mild CAD	40	53	35	47	75		
Moderate CAD	2	22	7	78	9		
Severe CAD	1	33	2	67	3		

hs-CRP, high-sensitivity C-reactive protein; CAD, coronary artery disease; SVD, single vessel disease; DVD, double vessel disease; TVD, triple vessel disease; LMCA, left main coronary artery.

Table VI. Syntax score and number of affected vessels with respect to hs-CRP value.

	hs-CRP <0.5 mg/dl		hs-CRP ≥0.5 mg/dl			
Parameter	Mean	SD	Mean	SD	Mean difference	P-value
No. of vessels	1.65	0.75	2.09	0.77	-0.440	0.009
Syntax score	11.06	7.54	15.26	8.84	-4.203	0.019

hs-CRP, high-sensitivity C-reactive protein; SD, standard deviation.

present study a weak correlation of hs-CRP with TIMI score (r=0.131, P=0.073) was observed. Foussas *et al* (21) suggested the prognostic usefulness of hs-CRP levels along with the well-validated TIMI risk score for STEMI and non-STEMI.

Increased hs-CRP values correlate with other risk scores in ACS. In one study, Schiele *et al* (22) demonstrated an independent predictive role of CRP in ACS patients; patients in the highest quartile of CRP showed increased mortality rates at 30 days of follow-up. Hence, in a setting of ACS, the hs-CRP value may be combined with well-validated risks such as TIMI and Global Registry of Acute Coronary Events scores, and helps in better predicting adverse events. In the present study 77 (40%) patients with acute STEMI admitted with a window period of 0-6 h had hs-CRP values <0.5 mg/dl, and there was no significant difference in hs-CRP values between different types of MI. These findings accorded well with the study by Cristell *et al* (23), which reported that 41% of patients admitted <6 h from symptom onset had hs-CRP

Table VII. In-hospital complications.

Complications	N	Mean hs-CRP (mg/dl)	SD	SE of mean	95% CI for mean		Min	Max	P-value
					Lower bound	Upper bound			
LV dysfunction									0.328
Absent	25	0.67	1.00	0.20	0.25	1.08	0.02	4.98	
Affected	165	0.71	0.76	0.06	0.60	0.83	0.01	4.67	
Heart failure									0.267
Absent	160	0.70	0.82	0.06	0.57	0.83	0.01	4.98	
Affected	30	0.74	0.61	0.11	0.51	0.97	0.05	2.53	
Shock									0.094
Absent	178	0.70	0.81	0.06	0.58	0.82	0.01	4.98	
Affected	12	0.85	0.48	0.14	0.54	1.15	0.14	1.80	
Acute MR									0.031
Absent	176	0.69	0.80	0.06	0.57	0.81	0.01	4.98	
Affected	14	0.97	0.67	0.18	0.58	1.35	0.20	2.53	
VSR									-
Absent	188	0.71	0.79	0.06	0.60	0.82	0.01	4.98	
Affected	1	0.33	-	-	-	-	0.33	0.33	
Bradyarrythmias									0.349
Absent	176	0.70	0.81	0.06	0.58	0.82	0.01	4.98	
Affected	14	0.76	0.55	0.15	0.44	1.07	0.14	1.80	
Tachyarrythmias									0.120
Absent	179	0.70	0.80	0.06	0.58	0.81	0.01	4.98	
Affected	11	0.90	0.64	0.19	0.47	1.33	0.20	2.26	
Recurrent angina									0.459
Absent	187	0.71	0.80	0.06	0.59	0.82	0.01	4.98	
Affected	3	0.74	0.32	0.18	-0.06	1.53	0.39	1.02	
LV thrombus									0.097
Absent	188	0.71	0.79	0.06	0.60	0.83	0.01	4.98	
Affected	2	0.13	0.11	0.08	-0.83	1.08	0.05	0.20	

hs-CRP, high-sensitivity C-reactive protein; SD, standard deviation; SE, standard error; CI, confidence interval; LV, left ventricular; MR, mitral regurgitation; VSR, ventrical septal rupture.

values <2 mg/l (23). The same study showed a wide dispersion of hs-CRP values, largely overlapping with those of control subjects and authors could not explain the exact reason for hs-CRP values <2 mg/l in 41% of STEMI patients. Similar findings of a very wide dispersion of hs-CRP values were reported in the control subjects of the PROVE IT-TIMI 22 study, which was found to be unrelated to LDL cholesterol levels (24). In the present study, with regard to window period, a greater number of patients presented with hs-CRP values >0.5 mg beyond 6 h (P=0.05). The mechanism for CRP elevation and its predictive value for different outcomes in patients with ACS depend critically upon the clinical setting and time of measurement (8,25).

The Syntax score is a comprehensive angiographic scoring system derived entirely from the coronary anatomy and lesion characteristics (26-28). In the present study, the hs-CRP values were shown to be positively correlated with Syntax score (r=0.285, P=0.007). Higher Syntax scores were associated with high hs-CRP values (mean hs-CRP value for a score ≤22 was 0.59 vs. 2.11 mg/dl for a score ≥33). To the best of our knowledge, there are no previous studies correlating hs-CRP with Syntax score in STEMI. However, a few studies have correlated it with the presence and extent of severity of CAD in ACS; the present study findings corroborate earlier studies, which have shown a correlation between CRP and the severity of CAD (29,30).

Zebrack *et al* (29) reported a weak association between CRP and CAD score. In view of their result, they suggested that CRP could determine primary plaque properties (that is, inflammation and instability), whereas CAD score could identify the extent of the atherosclerotic plaque.

In an another study, Arroyo-Espliguerol *et al* (31) showed a significantly higher hs-CRP value in patients with ACS compared with chronic stable angina (P=0.004) and a

Table VIII. hs-CRP and mortality.

	hs-CRP <0.5 mg/dl		hs-CRP ≥0.5 mg/dl				
Mortality	N	%	N	%	Total	χ^2	P-value
In-hospital mortality						0.273	0.601
Absent	88	51	86	49	174		
Affected	7	44	9	56	16		
30 day mortality						1.006	0.316
Absent	87	50	88	50	175		
Affected	1	100	0	0	1		

hs-CRP, high-sensitivity C-reactive protein.

correlation with complex angiographic lesions (P=0.001). Similar findings were reported by Azar *et al* (32) in an angiographic study. However, Rifai *et al* (33) did not find any significant association between inflammatory markers and CAD.

With regard to various complications, although mean hs-CRP values were higher in the presence of various complications, there was no significant difference of hs-CRP values according to the presence or absence of a complication, with the exception of patients who developed mitral regurgitation, where there was a significant difference between mean hs-CRP values. It is possible that the values for various complications may reach statistical significance when a larger sample size is used. In the present study there was no statistically significant difference observed between mean hs-CRP values in patients with or without in-hospital mortality; this could be explained by the small study sample size. However, there are multiple studies which have demonstrated an increased mortality rate in patients with STEMI and increased hs-CRP (34-38).

The cross-sectional nature and relatively small study sample are obvious limitations of the present study. Because of this, the study could not establish causality and could only establish an association. With difficulties in confirming the external validity of the results, the conclusions derived from this study must be considered preliminary and hypothesis-generating.

Inflammation plays an important role in atherothrombosis, and the measurement of inflammatory markers, specifically hs-CRP, might provide a novel method for detecting individuals with a high risk of plaque rupture in ACS. hs-CRP measurement is a valuable tool in STEMI patients. This study highlighted the association of increased hs-CRP value with higher Killip class, higher TIMI score, and most importantly with higher Syntax score, which indicates an overall atherosclerotic burden of coronary arteries. The present study has also demonstrated an association of higher hs-CRP values with increased hospital complications, and increased short- and long-term mortality. It is also considered that the highlighted role of inflammation in this study will increase understanding of atherosclerosis in general and should have clinical applications in therapy targeting for this serious disease.

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