

## Original Article

# *Relationship Between High-Sensitivity C-Reactive Protein and Left Ventricular Perfusion and Function by ECG-Gated SPECT Myocardial Perfusion Imaging*

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## ABSTRACT

**Background:** We sought to evaluate the relationship between left ventricular (LV) perfusion and function assessed by ECG-gated single-photon emission computerized tomography (SPECT) myocardial perfusion imaging (MPI) and serum high-sensitivity C-reactive protein (hs-CRP).

**Methods:** The images of 86 patients were reviewed for perfusion/functional defects by visual (subjective) interpretation. Quantitative (objective) LV measurements, including summed stress score (SSS), were calculated with the quantitative gated SPECT/quantitative perfusion SPECT (QGS/QPS) software. Via the quantitative method, the patients were categorized into an SSS<4 group (normal LV perfusion) and an SSS≥4 group (abnormal LV perfusion).

**Results:** There was no significant difference regarding the mean (±SD) hs-CRP level between normal (1.54±1.6 mg/L) and abnormal (1.88±2.61 mg/L) LV perfusions assessed by visual interpretation ( $P=0.493$ ). However, by the quantitative (objective) method, the mean (±SD) hs-CRP level was significantly higher in the SSS≥4 group than in the SSS<4 group (1.36±2.08 vs 2.37±2.37;  $P=0.04$ ). Receiver operating characteristic curve analysis (cutoff value =1 mg/L) distinguished patients with an SSS of 4 or greater with a sensitivity of 69% and specificity of 70% (area under the curve =0.71;  $P=0.001$ ).

**Conclusions:** The hs-CRP level had acceptable sensitivity and specificity to determine LV perfusion defects by the objective method but not by the subjective assessment (visual method) of LV perfusion defects. (*Iranian Heart Journal 2021; 22(4): 90-100*)

**KEYWORDS:** Single-photon emission computed tomography (SPECT), Myocardial perfusion imaging, Coronary artery disease, C-reactive protein

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Myocardial perfusion imaging (MPI) with single-photon emission computerized tomography (SPECT) to determine ventricular function is an important imaging stress test in the risk stratification of ischemic heart disease. SPECT-MPI can be applied for both those with and without coronary artery disease (CAD).<sup>1-3</sup> A normal stress perfusion has a high negative predictive value for myocardial infarction (MI) and cardiac death,<sup>4</sup> and MPI provides acceptable long-term prognostic value for cardiac events.<sup>5, 6</sup> Additionally, patients with abnormal SPECT MPI extent of the abnormality are more likely to experience MI, cardiac death,<sup>7</sup> and major adverse cardiovascular events (MACE).<sup>8-10</sup> In particular, perfusion defects of more than 10% of the left ventricle (LV) have a cardiovascular mortality rate of 2% per year, much higher than the rate in those without such defects. Further, MPI and the extent of scar identified can improve survival by deciding between early revascularization and medical therapy.<sup>11</sup>

Another component that has gained considerable attention in cardiovascular diseases is inflammation. In this regard, research has focused on high-sensitivity C-reactive protein (hs-CRP), interleukins 6 and 17, neopterin, and high-sensitivity troponin T (hs-TnT).<sup>12, 13</sup> Previous investigations have shown that hs-CRP is directly associated with atherosclerosis,<sup>14</sup> reduced coronary flow reserve,<sup>15</sup> and coronary lesion severity.<sup>16</sup> Accordingly, hs-CRP and other inflammatory markers have been suggested to be included in risk stratification models.<sup>17</sup> Nonetheless, debate on the advantages and disadvantages of hs-CRP continues.<sup>18</sup>

There is evidence that the hs-CRP level is increased in patients with mild-to-moderate myocardial perfusion defects<sup>19</sup> and patients with a slow coronary flow.<sup>20</sup> A report

demonstrated that hs-CRP and hs-TnT were able to recognize cardiac health by SPECT-MPI and that their levels were significantly higher in those with LV perfusion abnormalities.<sup>21</sup> In contrast, another study on patients with symptomatic CAD did not find differences with regard to hs-CRP between normal (2 mg/L) and abnormal (2.2 mg/L) MPI.<sup>1</sup>

As the measurement of hs-CRP is accessible in most medical centers and is easily done, we hypothesized that the hs-CRP level could be associated with LV perfusion and functional abnormalities on MPI.

## METHODS

### Study Design and Setting

The present cross-sectional analytic study was performed in our academic nuclear medicine center from 2015 through 2016.

### Study Population and Eligibility Criteria

The study population consisted of patients for whom the necessity of performing gated SPECT-MPI had been established by cardiologists. All these patients had CAD risk factors or established CAD. The exclusion criteria were composed of cardiac valvular diseases, myocardial conditions, LV hypertrophy, left bundle branch blocks, arrhythmias, heart failure defined as an LV ejection fraction below 41% by 2D transthoracic echocardiography in the past 1 month, acute coronary syndromes, revascularization (percutaneous coronary interventions or coronary artery bypass grafting surgery) within the preceding 6 months, uncontrolled hypertension (systolic blood pressure >210 mm Hg and/or diastolic blood pressure >120 mm Hg), major surgery in the preceding 6 months, trauma, major acute/chronic infections, malignancies, systemic conditions (eg, renal, hepatic, rheumatic, inflammatory, and peripheral vascular diseases), and thyroid disturbances.

### Sampling

Sampling was performed via the convenience sampling method, and 60 patients were selected from the eligible study population.

### Variables

A data collection form was designed to gather the required data, including demographic information, height, weight, body mass index, conventional CSD risk factors, chest pain, exertional dyspnea, and medication history.

### SPECT-MPI

SPECT-MPI using Tc 99m sestamibi was performed according to a 2-day protocol at rest and exercise. The images were interpreted via the visual (subjective) method by 2 experienced nuclear medicine specialists, who were blinded to hs-CRP measurements. Abnormal perfusion was defined as a reversible and/or irreversible perfusion defect confirmed by the specialists. In the quantitative (objective) method, summed stress score (SSS) was used. In addition, other quantitative indices, including peak filling rate (PFR), LV ejection fraction, end-systolic volume (ESV), end-diastolic volume (EDV), and time to peak filling (TTPF), were recorded. The patients were requested to fast for at least 4 hours before MPI to prevent an increased blood flow to the intestines and the absorption of radioactive isotopes. They were only allowed to take non-caffeinated and non-dairy drinks. Caffeinated drinks were prohibited for at least 24 hours before MPI. For patients without a CAD history, beta-blockers and calcium channel blockers were prohibited as these agents can reduce the diagnostic sensitivity of MPI.

On the first day, stress testing was done by inducing stress through treadmill exercise or pharmacologically with dipyridamole. The heart rate and blood pressure (systolic and

diastolic) of the patients were recorded. In exercise stress, according to the Bruce protocol, the patients first started treadmill exercise. Then when their heart rate reached 85% of the expected maximum heart rate (220/min-age) or if the indications to terminate the stress test were met, Tc 99m sestamibi (20 mCi) was injected, and the stress test was continued for 1 to 2 minutes. If a patient was not able to exercise and there were no contraindications, intravenous dipyridamole (0.142 mg/kg/min or 0.56 mg/kg) was injected over 4 minutes. Thereafter, 3 to 4 minutes later, Tc 99m sestamibi (20 mCi) was injected. The next day, SPECT-MPI was done at rest through the injection of Tc 99m sestamibi (20 mCi). For image acquisition, a dual-head gamma camera (Symbia T2, Siemens Healthcare), equipped with CT-attenuation correction, was used. The image acquisition (ECG-gated) was done 15 minutes after treadmill exercise and 45 minutes after dipyridamole injection. Image acquisition (ECG-gated) at rest was done for 32 patients, but it was not performed for the others due to various reasons including arrhythmia. The patients were scanned in the supine position with their arms over the head. First, CT with a small radiation dose was obtained (15 mAs and 130 kVp) to determine the isotope absorption map. Next, ECG-gated SPECT-MPI with 16-frame gating was performed in each cardiac cycle by employing a 20% window centered over a photopeak of 140 keV. The images were obtained with 180° rotation (−45° left posterior oblique to 135° right anterior oblique) by the step-and-shoot method with 64×64 matrix and 32 views. (Each view lasted for 25 seconds.) All the images were first segmented by Quantitative Gated SPECT/Quantitative Perfusion SPECT (QGS/QPS) software packages (version 0.4, May 2009).<sup>22</sup> Then, the contours of the images were reviewed case-by-case by the readers. Cases with artifacts

in the automatically drawn region of interest (ROI) that could not be manually adjusted were excluded. After the reconstruction of the images by the filtered back-projection method using the Butterworth filter, the quantification of LV perfusion and function was done by QGS/QPS software packages in both stress and rest phases. Perfusion quantitative indices, including total perfusion deficit (TPD), summed rest score (SRS), summed difference score (SDS), and SSS, were reviewed. Additionally, LV functional indices, including PFR, PFR2, TTPF, EF, EDV, ESV, and mean filling rate (MFR/3), were extracted. All the images were reviewed by 2 experienced specialists in MPI both via subjective visual interpretation and quantitatively using a standard 17-segment model proposed by the American Heart Association. SSS was calculated by the automatic summing of all 17 segments in the stress phase. SRS was similarly calculated by summing all the scores of 17 segments in the rest phase. The difference between SSS and SRS was termed "SDS".

### Measurement of hs-CRP

After an overnight fast and before SPECT-MPI, blood samples were obtained and hs-CRP was measured by latex turbidimetric immunoassay. The lowest detectable concentration of hs-CRP with this method was 0.15 mg/L.

### Association Between LV Perfusion and Function and hs-CRP

First, the patients were categorized into 2 groups of normal and abnormal MPI based on the findings of the visual interpretation method, and hs-CRP and other variables were compared between these 2 groups. Then, according to quantitative variables extracted by QPS, the patients were categorized into an  $SSS < 4$  group (normal) and an  $SSS \geq 4$  group (abnormal), and hs-

CRP was compared between these 2 groups. Subsequently, the abnormal SSS group was further categorized into mild ( $4 \leq SSS \leq 8$ ), moderate ( $9 \leq SSS \leq 13$ ), and severe ( $SSS > 13$ ), and hs-CRP was compared between these 3 groups.

### Statistical Analysis

Descriptive indices, including frequencies, percentages, and the mean  $\pm$  the standard (SD), were used to express the data. For the comparison of the frequencies of categorical variables between the normal and abnormal LV perfusion groups, the  $\chi^2$  test or the Fisher exact test was utilized. For the comparison of continuous variables between the normal and abnormal MPI groups, the *t* test or Mann-Whitney test was employed. The Pearson correlation test was used to find any correlation between the hs-CRP level and the quantitative measurements. A linear regression analysis was done to find any association between the hs-CRP level and the quantitative measurements of LV perfusion and function. The receiver operating characteristic (ROC) curve was applied to determine the best cutoff value for hs-CRP to differentiate normal from abnormal LV perfusion assessed by the visual method. A *P*-value of less than 0.05 was considered statistically significant. All the analyses were performed with the SPSS software, version 20.0 (IBM, US).

### Ethics

The study protocol was approved by the ethics committee of our medical university. The objectives of the study were explained to the patients, and written informed consent was obtained prior to enrollment. The study was in conformity with the Declaration of Helsinki.

## RESULTS

### General Characteristics

A total of 133 patients were entered into the study. From this total, 47 patients were

excluded due to low-quality MPI images, no gated study in the stress phase (due to arrhythmia and various reasons), and problems in blood hs-CRP measurement (hemolysis). Ultimately, 86 patients remained for the analyses. In 54 patients, ECG-gated MPI was not done in the rest phase due to human error or no high-quality gated study. Therefore, the required data of ECG-gated MPI in the rest phase were only available for 32 patients.

The 86 patients were comprised of 68 male (79.1%) and 18 female (20.9%) patients at a mean ( $\pm$ SD) age of 55.41 ( $\pm$ 11.38) years (range =26–83 y). The mean ( $\pm$ SD) body mass index was 27.80 ( $\pm$ 5.50) kg/m<sup>2</sup>. The mean ( $\pm$ SD) of heart rate, SBP, and DBP was 76.23 ( $\pm$ 14.11)/min, 132.1 ( $\pm$ 13.88) mm Hg, and 83.78 ( $\pm$ 8.11) mm Hg, respectively.

### Normal and Abnormal MPI

Out of the 86 patients, 49 patients (57%) had abnormal MPI. Table 1 summarizes clinical variables, CAD risk factors, and medication history in total as well as in the normal and abnormal MPI groups. No significant differences existed between the normal and abnormal MPI groups regarding sex and CAD symptoms and risk factors except for hyperlipidemia, which was more frequent in the abnormal MPI group. As a result, statins were more frequently used in this group. Some other medications, including proton pump inhibitors, diuretics, and clopidogrel, were recorded; nevertheless, their frequency was too low to be presented in Table 1. The mean ( $\pm$ SD) hs-CRP level was 1.74 (2.23) mg/L in the 86 patients. There was no significant difference regarding the mean (SD) hs-CRP level between the normal MPI group and the abnormal MPI group (1.54 $\pm$ 1.6 mg/L vs 1.88 $\pm$ 2.61 mg/L;  $P=0.493$ ).

### Stress Test

The exercise stress test was done for 52 patients. In 34 cases (39.5%), exercise stress

was not amenable and intravenous dipyridamole was injected. The minimum and maximum total exercise times were 4 and 10 minutes, respectively (mean=7.96 min). There was no significant difference in the total stress (exercise) time between the normal MPI group and the abnormal MPI group (53.7 $\pm$ 12.74 min vs 56.69 $\pm$ 10.18 min;  $P=0.079$ ). Stress test times with dipyridamole were also comparable between the normal and abnormal LV perfusion groups. Table 2 presents the stress test results (exercise and dipyridamole) in the normal and abnormal MPI groups.

### Quantitative Measurement, MPI, and hs-CRP

Table 3 shows comparisons of quantitative measurements between the normal and abnormal LV perfusion groups defined by the visual method. The mean ( $\pm$ SD) SRS was significantly lower in the normal LV perfusion group than in the abnormal LV perfusion group (0.54 $\pm$ 0.87 vs 1.94 $\pm$ 3.86;  $P=0.034$ ). In addition, TPD in the stress and rest phases was lower in the normal LV perfusion group. The Pearson correlation test showed a significant correlation only between hs-CRP and PER and EDV in the stress phase. There were no other significant associations between hs-CRP and the quantitative measurements. Regression analysis also found no association between hs-CRP and the LV perfusion and function measurements. Table 4 shows the hs-CRP level in the 2 SSS groups (SSS=0–3 and SSS $\geq$ 4). As can be seen, the mean hs-CRP level was significantly higher in the SSS $\geq$ 4 group than in the SSS<4 group ( $P=0.04$ ). No significant difference existed between the SSS<4 and SSS $\geq$ 4 groups regarding CAD risk factors and medications, including statins. ROC curve analysis to evaluate the diagnostic accuracy of hs-CRP in diagnosing patients with SSS $\geq$ 4 showed that an hs-CRP level of 1 mg/L had a sensitivity of 69% and

a specificity of 70% (AUC=0.71;  $P=0.001$ ). ROC curve analysis to detect diastolic dysfunction (TTPF>207 and PFR<1.7) in the

stress phase was performed, but the result was not statistically significant (Fig. 1).

**Table 1.** Sex, CAD risk factors, and medication history in total as well as in the normal and abnormal LV perfusion groups (visual interpretation) among 86 patients who underwent ECG-gated SPECT-MPI

Variables		Total (N=86)	Normal LV Perfusion (n=37)	Abnormal LV Perfusion (n=49)	Sig.
Sex	Male	68 (79.1%)	26 (70.3%)	42 (85.7%)	0.071
	Female	18 (20.9%)	11 (29.7%)	7 (14.3%)	
Chest Pain	Typical	8 (9.3%)	1 (2.7%)	7 (14.3%)	0.068
	Atypical	49 (57%)	23 (62.2%)	26 (53.1%)	0.267
	Non-anginal	4 (4.7%)	3 (8.1%)	1 (2%)	0.21
Exertional dyspnea		37 (43%)	19 (51.4%)	18 (36.7%)	0.128
CAD Risk Factors	DM	12 (14%)	5 (13.5%)	7 (14.3%)	0.588
	Hypertension	32 (37.2%)	12 (32.4%)	20 (40.8%)	0.285
	Hyperlipidemia	27 (31.4%)	7 (18.9%)	20 (40.8%)	0.025
	Previous MI	2 (2.3%)	0	2 (4.1%)	0.322
	Smoking	1 (1.2%)	0	1 (2%)	0.462
	Family history of CAD	10 (11.6%)	2 (5.4%)	8 (16.3%)	0.109
Medications	NSAIDs	13 (15.1%)	5 (13.5%)	8 (16.3%)	0.482
	ACEI	4 (4.7%)	2 (5.4%)	2 (4.1%)	0.579
	Statins	10 (11.6%)	1 (2.7%)	9 (18.4%)	0.024
	Beta-blockers	12 (14%)	4 (10.8%)	8 (16.3%)	0.343
	Nitrates	3 (3.5%)	0	3 (6.1%)	0.180

LV, Left ventricle; ECG, Electrocardiography; SPECT, Single-photon emission computerized tomography; MPI, Myocardial perfusion imaging; DM, Diabetes mellitus; CAD, Coronary artery disease; NSAID, Non-steroidal anti-inflammatory drug; ACEI, Angiotensin-converting enzyme inhibitor

**Table 2.** Stress test (exercise and dipyridamole) in the normal and abnormal LV perfusion groups in 84 patients who underwent SPECT-MPI

		Total	Normal LV Perfusion	Abnormal LV Perfusion	P-value
Exercise Stage	Stage 1	0	0	0	0.062
	Stage 2	9 (17.6%)	6 (27.3%)	3 (10.3%)	
	Stage 3	36 (70.6%)	15 (68.2%)	21 (72.4%)	
	Stage 4	5 (9.8%)	0	5 (17.2%)	
	Stage 5	1 (2%)	1 (4.5%)	0	
Stress	Exercise	52 (60.5%)	23 (62.2%)	29 (59.2%)	0.48
	Dipyridamole	34 (39.5%)	14 (37.8%)	20 (40.8%)	

LV, Left ventricle; SPECT, Single-photon emission computerized tomography; MPI, Myocardial perfusion imaging

**Table 3.** Comparison of the quantitative measurements of LV perfusion and function between the normal and abnormal MPI groups in 84 patients who underwent SPECT-MPI

		Abnormal LV Perfusion	Normal LV Perfusion	Total	P-value
		Mean±SD	Mean±SD	Mean±SD	
SSS		4.61±6.95	2.38±2.48	3.65±5.58	0.066
SRS		1.94±3.86	0.54±0.87	1.34±3.04	0.034
SDS		2.80±3.95	1.87±2.17	2.41±3.32	0.213
TPD	Stress	5.86±9.95	2.32±2.27	4.34±7.82	0.037
	Rest	3.90±5.12	1.97±1.99	3.07±4.17	0.033

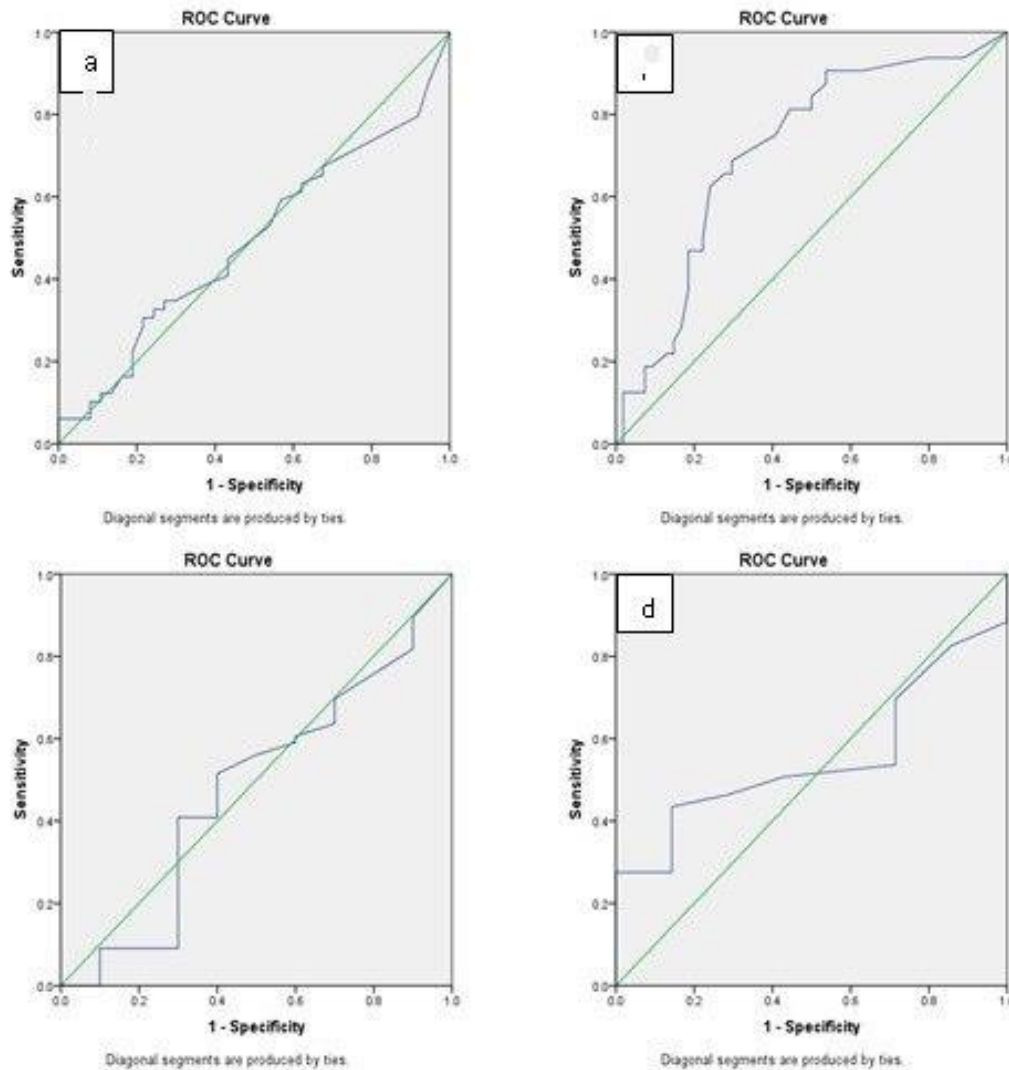
	Difference	1.90±6.87	0.32±2.97	1.22±5.57	0.196
SMS	Stress	3.76±6.51	1.46±1.90	2.77±5.17	0.041
	Rest	4.55±5.78	0.83±1.27	3.16±4.95	0.037
	Difference	-0.70±3.79	0.67±1.56	-0.19±3.18	0.245
STS	Stress	1.82±3.81	0.95±1.75	1.44±3.11	0.200
	Rest	2.95±3.65	1.83±2.48	2.53±3.26	0.357
	Difference	-0.30±3.65	-0.33±1.07	-0.31±2.92	0.976
EDV	Stress	75.50±18.38	72.42±23.25	74.17±20.54	0.498
	Rest	78.45±14.59	90.08±36.13	82.81±25.03	0.208
	Difference	-0.6±7.70	-8.42±10.64	-3.53±9.56	0.022
ESV	Stress	26.06±12.23	23.03±12.73	24.76±12.47	0.266
	Rest	28±11.72	33.25±18.94	29.97±14.78	0.339
	Difference	0.25±6.50	-5.25±7.06	-1.81±7.13	0.032
EF	Stress	66.74±9.64	69.46±11.78	67.91±10.63	0.242
	Rest	65.45±9.17	65.67±9.91	65.53±9.30	0.950
	Difference	-1.10±6.91	-0.17±13.84	-0.75±9.87	0.800
PER	Stress	-3.42±0.69	-4.56±5.47	-3.89±3.54	0.171
	Rest	-3.12±0.56	-3.28±0.73	-3.18±0.62	0.503
	Difference	-0.10±0.65	-0.47±0.90	-0.22±0.75	0.205
PFR	Stress	2.30±0.74	2.78±0.77	2.49±0.78	0.010
	Rest	2.33±6.69	2.46±1.06	2.38±0.83	0.687
	Difference	0.11±0.56	0.45±0.93	0.22±0.71	0.231
PFR2	Stress	2.07±1.05	1.96±0.76	2.02±0.94	0.616
	Rest	11.92±33.23	1.22±0.45	7.91±26.54	0.276
	Difference	-10.19±33.32	0.54±1.03	-6.62±27.46	0.322
MFR/3	Stress	1.30±0.37	7.30±32.05	3.75±20.50	0.212
	Rest	1.40±0.42	26.89±58.88	10.96±37.25	0.060
	Difference	-0.01±6.34	3.73±75.18	1.24±41.92	0.823
TTPF	Stress	151.27±46.75	143.84±37.02	148.24±42.94	0.462
	Rest	168.80±24.06	147.30±15.81	161.63±23.73	0.016
	Difference	-13.70±38.80	-7.33±22.95	-11.72±34.36	0.653

LV, Left ventricle; SPECT, Single-photon emission computerized tomography; MPI, Myocardial perfusion imaging  
 TPD, Total perfusion deficit; SSS, Summed stress score; SRS, Summed rest score; SDS, Summed difference score;  
 EDV, End-diastolic volume; ESV, End-systolic volume; EF, Ejection fraction; TTPF, Time to peak filling; PFR, Peak  
 filling rate; SMS, Summed motion score; MFR, Mean filling rate; STS, Summed thickening score

**Table 4.** Comparison of the mean ( $\pm$ SD) hs-CRP levels between the 2 groups based on SSS

	SSS<4 (n=54)	SSS $\geq$ 4 (n=32)	P-value
hs-CRP, mg/L	1.36 ( $\pm$ 2.08)	2.37 ( $\pm$ 2.37)	0.04

SSS, Summed stress score; hs-CRP, High-sensitivity C-reactive protein



**Figure 1.** The images illustrate the receiver operating characteristic (ROC) curve analysis and associations between hs-CRP and visually interpreted MPI (a), summed stress score (SSS) (b), TTPF (time to peak filling) (c), and PFR (peak filling rate) (d).

## DISCUSSION

In the present study, we used SPECT-MPI to assess patients with suspected CAD and found that the measurement of hs-CRP had a significant association with the quantitative measurement of LV perfusion. Additionally, the serum hs-CRP level had acceptable sensitivity and specificity to distinguish perfusion defects characterized by an SSS of 4 or greater. Hence, we think that adding hs-CRP measurement to the management of candidates for MPI and using a cutoff value

of 1 mg/L can augment the diagnostic accuracy of MPI. In the detection of perfusion defects by visual interpretation, any defective perfusion is considered abnormal LV perfusion. However, the quantitative method has superiority in that it can divide patients into an SSS of 0 to 3 and an SSS of 4 or greater. By the visual interpretation of the scans, we identified 49 patients with abnormal LV perfusion, whereas the use of SSS helped us identify 32 patients with LV perfusion defects. Given the subjective nature of visual interpretation



and intraobserver variability, the repeatability of this method is lower than that of the quantitative method.<sup>23, 24</sup> It has been suggested that quantitative methods be drawn upon in clinical studies as this method is superior to visual interpretation.<sup>23</sup> Factors such as variations in visual interpretation and errors of software could be responsible. We think that this topic needs further studies to reveal differences between quantitative and visual interpretation methods.

Studies on the relationship between hs-CRP and LV perfusion defects are promising, although more studies are required to establish a clearer relationship. As serum hs-CRP measurement is accessible, these studies can provide invaluable information about its association with perfusion defects. Some researchers have investigated the role of hs-CRP in predicting cardiac health. In a previous study, a combination of hs-CRP (cutoff value <0.45 mg/L) and hs-TnT (cutoff value <3 ng/L) was found to have an estimated probability of 85% for cardiac health assessed by SPECT-MPI.<sup>21</sup> We included only candidates for SPECT-MPI who were suspected to have CAD. We found that about half of the patients had normal SPECT-MPI by the visual assessment of LV, and about one-third of the patients did not have functional/perfusion defects by quantitative assessment using QGS/QPS software packages. Thus, our results are somehow compatible with the reported results of the aforementioned study. A major difference is that we only studied hs-CRP, whereas the previous study combined cutoff values for both hs-TnT and hs-CRP, which had a better probability to predict cardiac health than each laboratory assessment alone. The 2 groups studied here based on visually interpreted LV perfusion did not have significant differences regarding CAD risk factors. As some studies have proposed a relationship between these risk factors and the hs-CRP level,<sup>25</sup> we can

conclude that these factors did not confound the observed findings.

Visual interpretation of SPECT-MPI is a standard in the interpretation of images, whereby the defect, size, and location of perfusion is reported. After visual interpretation, quantitative and quantitative analyses are done.<sup>26</sup> As was observed here, hs-CRP had a significant association only with quantitative analysis, but not with visual analysis. The usefulness of hs-CRP has been shown in inflammatory conditions, where inflammatory biomarkers are raised. In a previous study on patients with ankylosing spondylitis without CAD, it was reported that hs-CRP had a significant independent correlation with SPECT-MPI cardiac wall motion abnormalities.<sup>27</sup> Such studies support the idea that hs-CRP can be used in predicting cardiac health, a subject that has gained attention in the literature.<sup>21</sup> In our opinion, more studies are required for more definitive findings concerning the role of inflammatory markers to predict LV perfusion/functional defects and to find out whether such markers can replace the need for SPECT-MPI. These findings are still considered preliminary. Nonetheless, a combination of several inflammatory markers, including hs-CRP as the most eligible marker in detecting LV perfusion defects, can provide useful predictive information when patients with suspected CAD are evaluated.

The results of the current investigation should be interpreted by considering the following limitations. We only studied hs-CRP and were not able to include other inflammatory markers that are possible to correlate with abnormal LV perfusion such as hs-TnT and B-natriuretic peptide.

## CONCLUSIONS

The serum hs-CRP level had acceptable sensitivity and specificity to distinguish perfusion defects characterized by an SSS of

4 or greater. Adding hs-CRP measurement to the management of candidates for 16-frame ECG-gated SPECT-MPI and using a cutoff value of 1 mg/L could further the diagnostic accuracy of MPI in detecting perfusion defects.

### Ethical Considerations

There is no conflict of interest to declare regarding this article.

All the procedures performed were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent was obtained from all the participants included in the study.

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