

Diagnostic Accuracy Assessment of ST-Segment Displacements, Chest Pain and Stress Myocardial Perfusion Imaging Exercise Test in Coronary Stenosis Compared with Angiography Findings

Feridoon Rastgou MD¹, Ahmad Bitarafan-Rajabi MD¹, Ahmad Farhzadi MD¹, Nahid Yaghoobi MD¹, Hasan Firoozabady MD¹, Hadi Malek MD¹, Hossein Ali Basiri MD¹, Hassan Moladoust²

Abstract

Introduction- Nowadays, myocardial perfusion imaging (MPI) plays an important role in the early diagnosis of patients with coronary artery disease (CAD). This study sought to assess the performance of MPI alongside chest pain and ST-segment changes during the stress test by comparison with angiography in the diagnosis of coronary artery stenosis. To that end, the accuracy of these modalities in terms of sensitivity and specificity and the degree of agreement between their results in the diagnosis of coronary artery stenosis were evaluated.

Methods and Materials- The study population, selected from those with known or suspected CAD, was comprised of 85 patients (67 males) at a mean age of 53.7 ± 9.6 years. All the patients were subjected to SPECT imaging of the blood supply to the heart muscle during a two-day state of stress (either pharmacologically with Dipyridamole or through exercise test) and during rest via the injection of 99m Tc - MIBI. ST-segment changes during stress as well as clinical symptoms were recorded. All the patients underwent coronary angiography within two weeks, and coronary artery stenosis $>50\%$ was considered positive. Finally, the results of chest pain, ECG changes, and MPI for the evaluation of coronary artery involvement were compared with those of angiography as the gold standard.

Results- Of the 85 patients, who underwent angiography, 10 patients had normal coronary angiography, 22 single-vessel disease, 28 two-vessel disease, and 25 three-vessel disease. ST-segment depression and ST-segment elevation were observed in 40 and 6 patients, respectively. The ECG had sensitivity of 57% and specificity of 70% in the diagnosis of coronary artery stenosis. Fifteen patients had chest pain during stress; all of them had coronary involvement according to angiography. Of the 70 patients with no chest pain, coronary angiography was positive in 62 cases; accordingly, chest pain had sensitivity of 20% and specificity of 100% in the diagnosis of coronary artery stenosis. There were 80 patients with abnormal MPI, including 387 fixed and reversible defects. Therefore, MPI had sensitivity of 79%, specificity of 70%, and diagnostic accuracy of 76% in the diagnosis of coronary artery stenosis.

Conclusion- MPI enjoyed higher diagnostic accuracy and agreement coefficient than did chest pain and ST-segment changes in the diagnosis of coronary artery stenosis. Given the acceptable results of MPI in the diagnosis of coronary artery stenosis, this modality could be valuable in the management of CAD patients (*Iranian Heart Journal 2011; 12 (4):30-36*).

Keywords: ST-segment changes ■ Myocardial perfusion ■ Chest Pain ■ Coronary stenosis ■ Angiography

Received June. 13, 2011; Accepted for publication Feb. 10, 2012

1-Nuclear Medicine Department, Rajaei Cardiovascular, Medical & Research Center; Tehran University of Medical Sciences, Tehran, Iran Vali-Asr Ave., Niyayesh Blvd.

2-Guilan University of Medical Sciences, Rasht, Iran,

Correspondence: Ahmad Bitarafan-Rajabi Rajaei Cardiovascular, Medical & Research Center; Tehran University of medical sciences, Tehran, Iran Vali-Asr Ave., Niyayesh Blvd. email: bitarafan@hotmail.com abitarafan@yahoo.com

Coronary artery disease (CAD) is a major cause of death worldwide. CAD is a complex degenerative disease which gradually progresses with age. In America, the cardiovascular disease mortality is up to one million each year, half of which is due to ischemic heart disease caused by atherosclerosis¹⁻⁴. Atherosclerosis reduces the diameter of coronary arteries and then reduces the myocardial perfusion⁵. Today, the cardiovascular disease mortality due to atherosclerosis has risen significantly, as attested to by the more precise assessment of risk factors via recent advances in diagnostic modalities¹⁻⁴. Over the past two decades, the exercise stress test with myocardial perfusion imaging (MPI) has played an important role in the diagnosis of atherosclerosis disease. Single Photon Emission Computed Tomography (SPECT) depicts the three-dimensional distribution of radiopharmaceutical tracers in the body, and MPI is viewed in the reorientation and reconstruction of horizontal long-axis, vertical long-axis, and short-axis slices⁸⁻⁶. Several factors can affect MPI, including the type of the stress imaging test protocol, the time of imaging in relation to the radiotracer injection, and the interval between injection and imaging. MPI can be used for myocardial ischemia diagnosis, prognosis, risk stratification, and it can also evaluate the outcome of thrombolytic therapies such as percutaneous transluminal coronary angioplasty (PTCA) and coronary artery bypass graft surgery (CABG)⁹.

Several studies have assessed the accuracy of diagnostic procedures such as chest pain and ST-segment changes during stress testing in the diagnosis of CAD.¹²⁻¹⁰

Recent developments in computer technology and software for myocardial perfusion have led to advances in SPECT imaging. The present study sought to assess the diagnostic accuracy of myocardial perfusion scintigraphy in the non-invasive diagnosis of coronary artery stenosis and compare the results with angiography as the gold standard.

Materials and Methods

Patients

This clinical study included 85 patients (67 males and 18 females) at a mean age of 53.7 ± 9.6 years. The patients were selected from those with known or suspected CAD. All the patients had coronary angiography within 2 weeks. In this study, the exclusion criteria included all patients with myocardial perfusion images containing disturbing extra-cardiac activity and motion artefacts. The important clinical factors of the patients, including blood pressure, triglyceride, cholesterol, blood sugar, smoking, stress testing results, and angiography results, were recorded. The study was performed in the Nuclear Medicine and Molecular Imaging Department of Rajaei Cardiovascular, Medical and Research Center, affiliated with Tehran University of Medical Sciences. The study protocol was approved by the institutional ethics committee, and written informed consent was obtained from all the patients.

SPECT imaging

SPECT imaging was acquired with DST Xli Sopha with double-head 90-degree and high-resolution, low-energy collimator. Detectors' rotation was 45 degrees right anterior-oblique (RAO) to 45 degrees left posterior-oblique (LPO) using detector rotation 180-degree orbit with the step and shoot mode. Symmetric 20% energy window with photo-peak at 140 keV of ^{99m}Tc was selected. Imaging matrix size was determined at 64×64 (pixel size = 0.66) and the magnification factor was 1.33. MPI SPECT was performed using a two-day stress (either pharmacologically with Dipyridamole or via exercise) and rest protocol for all the patients through the injection of 20 mCi ^{99m}Tc-MIBI. ST-segment changes during stress and clinical symptoms were registered. In this study, the indices of chest pain, ECG changes, and myocardial perfusion were compared to evaluate CAD. Angiographic findings were

employed as the gold standard for the assessment of coronary artery stenosis. All patients with stenosis $\geq 50\%$ were considered positive.

Statistical analysis

The sampling method in the present study was convenience sampling of the patients with known or suspected CAD who were referred to our department for MPI or stress test, all within one year. Using the true positive, false positive, true negative, and false negative results of the diagnostic modalities, their respective sensitivity, specificity, and diagnostic accuracy were calculated. To investigate the agreement between the results of MPI, angiography, ECG, and chest pain, the Cohen kappa statistic using SPSS software was used.

Results

Of the 85 patients, 10 had normal coronary angiography, 22 had single-vessel disease (SVD), 28 two-vessel disease (2VD), and 25 three-vessel disease (3VD). ST-segment depression was detected in 40 patients, and 6 patients had ST-segment elevation. The ECG had sensitivity of 57% and specificity of 70% in the diagnosis of coronary artery stenosis.

Based on the results of coronary angiography, 15 patients had chest pain during stress, and 70 patients had no chest pain. Coronary angiography was positive in 62 cases. Chest pain had sensitivity of 20% and specificity of 100% in the diagnosis of coronary artery stenosis. Eighty patients had abnormal myocardial perfusion, including 387 fixed and reversible defects. Therefore, MPI had sensitivity of 79%, specificity of 70%, and diagnostic accuracy of 76% in the diagnosis of coronary artery stenosis. (Table I).

According to the polar map into three vascular territories, sensitivity and specificity were 91% and 47% for the left anterior descending (LAD) artery, 91% and 67% for the left circumflex (LCX) artery, and 80%

and 69% for the right coronary artery (RCA) (Table II).

Table I. Demographic and clinical characteristics of patients in this study

	Data
Patient (n)	85
Sex (Male/Female)	67/18
Age (Years)	53.7 \pm 9.6
Weight (kg)	72.7 \pm 11
High (cm)	167 \pm 8.4
Coronary Risk Factors, n (%)	
Diabetes (%)	14 (16.5)
Smoking (%)	24 (28.12)
Triglyceride (%)	21 (24.7)
Hypercholesterolemia (%)	22 (25.9)
Family (%)	10 (11.8)
Hypertension (%)	27 (31.18)
Angiography: (abnormal/normal)	75/10
Coronary disease:	
1-Vessel Disease (%)	22 (26)
2-Vessel Disease (%)	28 (33)
3-Vessel Disease (%)	25 (29)
LAD (%)	70 (82)
RCA (%)	40 (47)
LCX (%)	43 (51)
Stress Test:	
Exercise	54
Dipyridamole	31
CHEST PAIN (%)	
With Chest Pain In Stress (%)	15
Without Chest Pain In Stress (%)	70

The results of the evaluation showed that there was insignificant agreement between chest pain and the findings of angiography in the diagnosis of coronary artery stenosis. There was a significant coefficient of consistency between the ST-segment changes and MPI in the diagnosis of coronary artery stenosis compared with the results of angiography. MPI had a better agreement

(0.508) compared with the ST-segment changes (0.448).

Table II. Results of sensitivity, specificity and diagnostic accuracy of ST-segment, chest pain and MPI in the diagnosis of coronary artery stenosis

	Sensitivity	Specificity	Accuracy	Kappa	P Value
ST Segment Changes	57%	70%	54%	0.448	0.000
Chest Pain (%)	20%	100%	30%	0.056	NS
Myocardial Perfusion					
LAD	91%	47%	83%	0.461	0.000
RCA	80%	70%	75%	0.485	0.000
LCX	67%	90%	71%	0.578	0.000
Average	79%	70%	76%	0.508	-

Results of sensitivity, specificity, and diagnostic accuracy showed that despite the comparable specificity for the diagnosis of coronary artery stenosis, the diagnostic accuracy of MPI was higher in comparison with ST-segment changes. Table 2 shows the high sensitivity MPI (79%) compared with ST-segment changes (57%). With respect to the use of MPI in the diagnosis of coronary artery stenosis, the LCX had higher agreement than did the LAD and RCA, whereas it had less sensitivity, which resulted in lower accuracy (71% for the LCX, 75% for RCA and 83% for LAD compared with MPI) (Table II). Fig. A-1 and B-1, respectively, depict normal and abnormal myocardial perfusion images.

Discussion

Angiography as invasive method is the gold standard method for the determination of coronary artery stenosis. In the present study, angiography was performed according to the standard protocol within a two-week period after MPI. Of course this method has some limitations. The main purpose of this study was to assess the diagnostic accuracy and

coefficient of agreement in MPI SPECT as a non-invasive method for the determination of coronary artery stenosis.

A

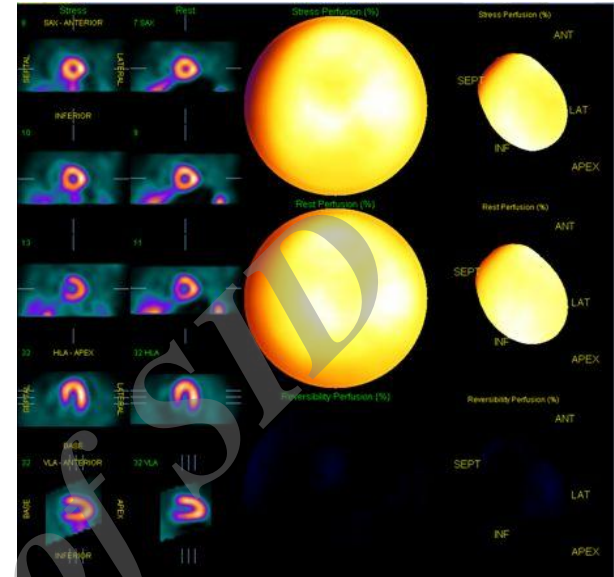
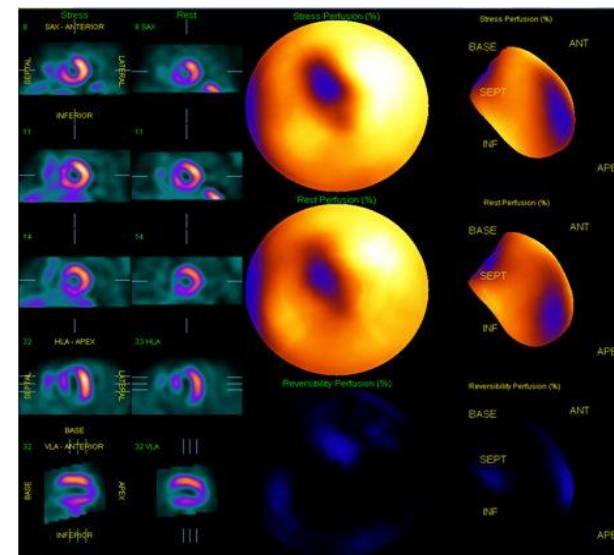


Fig. 1. normal (A) and abnormal (B) myocardial perfusion images.



(B)

Our results showed the sensitivity and specificity for the left anterior descending (LAD) artery were 91% and 47%, for the left circumflex (LCX) artery 91% and 67%, and for the right coronary artery (RCA) 80% and

69%, respectively; and the average sensitivity, specificity, and accuracy of MPI in the diagnosis of coronary artery stenosis were 79%, 70%, and 76%, respectively. Our case selection was not suitable to assess specificity because all the referred patients had a symptom and sign of ischemic heart disease. We know that some patients with a normal coronary have ischemic heart disease (IHD) such as endothelial dysfunction, coronary spasm, and insufficient coronary flow reserve. MPI is a sensitivity method for all IHD (with CAD and other causes of ischemia). On the other hand, our study was performed with a relatively old generation of the SPECT gamma camera and software. Today, new SPECT/CT gamma cameras with new software have more ability to determine the global and regional myocardial function (ejection fraction, end-diastole volume, end-systole volume, wall motion, wall thickness and thickening, phase analysis for assessment of dyssynchrony and quantitative perfusion defects such as sum stress score, and sum rest score).

However, some studies have shown different results. For example, in a study by Santoro et al. (1998) at the Institute of Cardiology in Italy on 235 patients, 95% sensitivity and specificity of 76% were reported¹³. In comparison with our results, although the sensitivity and specificity were higher, the difference in sensitivity is more noticeable. In another study, Elhendy et al. (2002) assessed the diagnostic accuracy of MPI dobutamine stress in 1208 patients with CAD: sensitivity, specificity, and accuracy were 85%, 72%, and 83%, respectively.¹⁴ Giorgetti et al. (2007) evaluated the diagnostic accuracy of myocardial gated SPECT in 120 patients with CAD and reported that sensitivity, specificity and accuracy were 78%, 72%, and 80%, respectively.¹⁵ Finally, Sato et al. in 2008 assessed the accuracy of the diagnosis of CAD over 70% using Coronary Angiography Computed Tomography (ACT) in comparison to MPI in 104 patients with CAD were respectively the sensitivity and specificity of

79%, 96% of CTA compared to 88% and 83%.¹⁶ In the study of Shin and et al. (2009) on 368 patients with diagnostic accuracy of CAD 50% and 70% using by prone MPI were respectively the sensitivity and specificity of 88%, 61% in the stenosis of coronary artery 50% and 92 %, 55% in the stenosis of coronary artery over 70%.¹⁸

On the other hand, Castell Conesa et al. (1997) studied 149 patients with coronary artery stenosis greater than 50%. They considered the diagnostic accuracy of the scan separately in three coronary arteries. Their results showed that the scan sensitivity and specificity were 85% and 74% for the LAD, 79% and 85% for the RCA, and 45% and 96% for the LCX, respectively.⁷ The Institute of Cardiology in Italy studied 235 patients with coronary artery stenosis greater than 50%. According to the type of the coronary artery separately, the sensitivity of the scans with the LAD was 71%, specificity 94%, sensitivity and specificity for the RCA 73% and 81%, sensitivity and specificity for the LCX 61% and 96%.¹³ In addition, Elherdy et al. (2006) studied 88 female patients with coronary artery stenosis: the diagnostic accuracy of the scan separately in all the three coronary arteries was considered. Their results showed that the scan sensitivity, specificity, and accuracy for the LAD was 82%, 84% and 83%, for RCA 77%, 84% and 81%, for LCX 74%, 80% and 78% and the average sensitivity, specificity and accuracy of 78%, 82% and 81%, respectively.¹⁷ Regarding the results of other studies, our investigation had accurate and acceptable results. As was mentioned above, all the cases were suspected or known CAD.

One important piece of software in MPI is quantitative perfusion SPECT (QPS). Parsad et al. (2010) evaluated ischemic area via the Change method in 997 patients with QGS and the sensitivity, specificity and accuracy were 90%, 81% and 85%, respectively¹⁹. With respect to the MPI result with new software and machine, today, for more accurate findings we need to use validation software

such as Cedars QPS, QGS, Emory Tool Box, and 4DMSPECT. Fortunately, all of the new machines (SPECT/CT) and new pieces of software are available in our department.

Reference

1. Stolzenberg J, London R. Reliability of stress thallium-201 scanning in the clinical evaluation of coronary artery disease. *Clin Nucl Med*. 1979 Jun; 4(6):225-8.
2. Abhyankar AD, Agrawal AG, Mehta AB. Recovery positive exercise stress test: an indication for coronary artery disease. *J Assoc Physicians India*. 1994 Sep; 42(9):700-2.
3. Marshall ES, Raichlen JS, Tighe DA, Paul JJ, Breuninger KM, Chung EK. ST-segment depression during adenosine infusion as a predictor of myocardial ischemia. *Am Heart J*. 1994 Feb; 127(2):305-11.
4. Pearlman JD, Boucher CA. Diagnostic value for coronary artery disease of chest pain during dipyridamole-thallium stress testing. *Am J Cardiol*. 1988 Jan 1; 61(1):43-5.
5. Waters DD, Szlachet J, Bourassa MG, Scholl JM, Thérout P. Exercise testing in patients with variant angina: results, correlation with clinical and angiographic features and prognostic significance. *Circulation*. 1982 Feb; 65(2):265-74.
6. Castell Conesa J, Santana Boado C, Candell Riera J, Aguadé Bruix S, Olona M, Canela T, García Burillo A, González JM, Domènech Torné FM, Soler Soler J. Stress myocardial gamma tomography in the diagnosis of multivessel coronary disease. *Rev Esp Cardiol*. 1997 Sep; 50(9):635-42.
7. Fragasso G, Lu C, Dabrowski P, Pagnotta P, Sheiban I, Chierchia SL. Comparison of stress/rest myocardial perfusion tomography, dipyridamole and dobutamine stress echocardiography for the detection of coronary disease in hypertensive patients with chest pain and positive exercise test. *J Am Coll Cardiol*. 1999 Aug; 34(2):441-7.
8. Kaul S, Senior R, Firschke C, Wang XQ, Lindner J, Villanueva FS, Firozan S, Kontos MC, Taylor A, Nixon II, Watson DD, Harrell FE. Incremental value of cardiac imaging in patients presenting to the emergency department with chest pain and without ST-segment elevation: a multicenter study. *Am Heart J*. 2004 Jul; 148(1):129-36.
9. Gimelli A, Rossi G, Landi P, Marzullo P, Iervasi G, L'Abbate A, and Rovai D. Stress/Rest Myocardial Perfusion Abnormalities by Gated SPECT: Still the Best Predictor of Cardiac Events in Stable Ischemic Heart Disease. *J Nucl Med* 2009; 50:546–553.
10. T Turer A, Mahaffey KW, Gallup D, Weaver WD, Christenson RH, Every NR and Ohman EM. Enzyme estimates of infarct size correlate with functional and clinical outcomes in the setting of ST-segment elevation myocardial infarction. *Current Controlled Trials in Cardiovascular Medicine* 2005, 6:12
11. Nakazato R, Tamarappoo BK, Kang X, Wolak A, Kite F, Hayes SW, Thomson L EJ, Friedman JD, Berman DS, and Slomka PJ. Quantitative Upright-Supine High-Speed SPECT Myocardial Perfusion Imaging for Detection of Coronary Artery Disease: Correlation with Invasive Coronary Angiography. *J Nucl Med* 2010; 51:1724–1731.
12. Paladugu N, Shaqra H, Blum S, Bhalodkar NC. Positive Vasodilator Stress ECG With Normal Myocardial Perfusion Imaging and Its Correlation With Coronary Angiographic Findings in African Americans and Hispanics. *Clin. Cardiol*. 33, 10, 638–642 (2010).
13. Santoro GM, Sciagrà R, Buonamici P, Consoli N, Mazzoni V, Zerauschek F, Bisi G, Fazzini PF. Head-to-head comparison of exercise stress testing, pharmacologic stress echocardiography, and perfusion tomography as first-line examination for chest pain in patients without history of coronary artery disease. *J Nucl Cardiol*. 1998 Jan-Feb; 5(1):19-27.
14. Elhendy A, Bax JJ, and Poldermans D. Dobutamine Stress Myocardial Perfusion Imaging in Coronary Artery Disease. *J Nucl Med* 2002; 43:1634–1646.
15. Giorgetti A, Rossi M, Stanislao M, Valle G, Bertolaccini P, Maneschi A, Giubbini R, De Rimini ML, Mazzanti M, Cappagli M, Milan E, Volterrani D, and Marzullo P. Feasibility and Diagnostic Accuracy of a Gated SPECT Early-Imaging Protocol: A Multicenter Study of the

Myoview Imaging Optimization Group. J Nucl Med 2007; 48:1670–1675.

16. Sato1 A, Hiroe M, Tamura1 M, Ohigashi H, Nozato T, Hikita H, Takahashi A, Aonuma K, and Isobe M. Quantitative Measures of Coronary Stenosis Severity by 64-Slice CT Angiography and Relation to Physiologic Significance of Perfusion in Nonobese Patients: Comparison with Stress Myocardial Perfusion Imaging. J Nucl Med 2008; 49:564–572.
17. Elhendy A, Schinke AFL, Bax JJ, van Domburg RT, Valkema R, Biagini E, Feringa HH, and Poldermans D. Accuracy of stress Tc-99m tetrofosmin myocardial perfusion tomography for the diagnosis and localization of coronary artery disease in women. J Nucl Cardiol 2006; 13:629-34.
18. Shin JH, Pokharna HK, Williams KA, Mehta R, and Ward RP. SPECT myocardial perfusion imaging with prone-only acquisitions: correlation with coronary angiography. J Nucl Cardiol 2009; 16:590–6.
19. Prasad M, Slomka PJ, Fish M, Kavanagh P, Gerlach J, Hayes S, Berman DS, and Germano G. Improved Quantification and Normal Limits for Myocardial Perfusion Stress–Rest Change. J Nucl Med 2010; 51:204–209.