

## Myocardial perfusion scintigraphy findings in patients with mild coronary atherosclerotic lesions on coronary angiography

### *Koroner anjiografisinde hafif aterosklerotik koroner lezyonu olan hastalarda miyokard perfüzyon sintigrafisi bulguları*

Zeki Dostbil<sup>1</sup>, Habib Çil<sup>2</sup>, Ebru Öntürk Tekbaş<sup>2</sup>, Zuhale Arıttürk Atılğan<sup>2</sup>, Yahya İslamoğlu<sup>2</sup>  
Bekir Taşdemir<sup>3</sup>, Yusuf Dağ<sup>1</sup>

Dicle University Medical Faculty, <sup>1</sup>Department of Nuclear Medicine and <sup>2</sup>Cardiology, Diyarbakir, Turkey

<sup>3</sup>Elazığ Training and Research Hospital, Department of Nuclear Medicine, Elazığ, Turkey

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#### ABSTRACT

**Objectives:** Myocardial perfusion scintigraphy (MPS) is widely used in functional assessment of myocardial perfusion. But, some study results are in contradiction with severity of coronary artery disease detected by coronary angiography (CA). It is frequently encountered case that CA is completely normal whereas MPS describes ischemia. In this study, we aimed to investigate whether mild atherosclerotic lesions cause ischemia.

**Materials and methods:** MPS with 99mTc-MIBI was performed in 52 patients who applied to cardiology clinics for history of chest pain and underwent diagnostic CA within 3 months.

**Results:** In 22 of 52 patients with mild atherosclerotic lesions, ischemia in various degrees was detected on MPS. In statistical analysis, any significant relationship was not found between ischemia and gender, hypertension, DM, dyslipidemia, smoking, mitral valve insufficiency, left ventricular hypertrophy, exercise testing result and affected coronary artery.

**Conclusion:** Our study findings have shown that mild atherosclerotic lesions even at very early stage may cause myocardial ischemia

**Key words:** coronary artery disease, myocardial ischemia, myocardial perfusion imaging, coronary angiography

#### INTRODUCTION

Myocardial perfusion scintigraphy (MPS) is a non-invasive modality widely used in evaluation of myocardial ischemia. Perfusion defects have been linked to areas supplied by significantly stenosed coronary arteries.<sup>1</sup> It has been also shown that perfusion ab-

#### ÖZET

**Amaç:** Miyokard perfüzyon sintigrafisi (MPS) miyokard perfüzyonunun fonksiyonel değerlendirilmesinde yaygın olarak kullanılmaktadır. Fakat bazı çalışma sonuçları koroner anjiyografi ile tespit edilen koroner arter hastalığının şiddeti ile zıtlık gösterir. Koroner anjiyografi tamamen normalken MPS'nde iskemiden bahsedilmesi sık karşılaşılan bir durumdur. Bu çalışmada, hafif aterosklerotik lezyonların iskemiye sebep olup olmadıklarını araştırmayı amaçladık.

**Yöntem ve Gereç:** Kardiyoloji Polikliniğine göğüs ağrısı şikayeti ile başvuran ve 3 ay içerisinde koroner anjiyografi yapılmış olan 52 hastaya 99mTc-MIBI ile miyokard perfüzyon sintigrafisi yapıldı.

**Bulgular:** Hafif derecede aterosklerotik lezyonu olan 52 hastanın 22'sinde MPS'de değişik derecelerde iske-mi bulguları gözlemlendi. Yapılan istatistik analizde iskemi ile cinsiyet, hipertansiyon, DM, dislipidemi, sigara içme, mitral kapak yetmezliği, sol ventrikül hipertrofisi, efor test sonucu ve aterosklerotik lezyonun bulunduğu damar arasında anlamlı bir ilişki tespit edilmedi.

**Sonuç:** Çalışma bulgularımız koroner arterlerdeki hafif aterosklerotik lezyonların, çok erken dönemlerde bile olsa, miyokarda iskemiye sebep olabileceğini göstermektedir.

**Anahtar kelimeler:** koroner arter hastalığı, miyokard iskemisi, miyokard perfüzyon görüntüleme, koroner anjiyografi

normality might be caused by angiographically nonsignificantly stenosed (<50% diameter stenosis) arteries.<sup>2,3</sup> Patients with reversible perfusion defects on MPS suggestive of ischemia but angiographically insignificant coronary artery disease have often been labeled as having a "false-positive" scan.<sup>1</sup>

**Yazışma Adresi /Correspondence:** Dr. Zeki Dostbil, Dicle University Medical Faculty, Department of Nuclear Medicine, Diyarbakir, Turkey. E-mail: zekidostbil@yahoo.com

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Recent studies with intravascular ultrasonography (IVUS) and microvascular function assessment have revealed the limitations of traditional coronary angiography (CA) and underestimation of atherosclerotic burden in areas of perfusion defects on MPS where microvascular and endothelial dysfunction were shown.<sup>2,4-7</sup>

In this study, we aimed to investigate myocardial ischemia findings on MPS in patients with angiographically mild atherosclerotic coronary lesions.

## MATERIALS AND METHODS

This study comprised of 52 patients in 'Elazig Research and Training Hospital' and 'Dicle University Medical Faculty, Department of Nuclear Medicine' between April 2008 and March 2010. The main indication for referral of all patients was evaluation of chest pain. Patients having LBBB, RBBB or muscle bridge that may cause false positive scintigraphy results were excluded from study.

In all patients, 99mTc-MIBI ECG Gated (8-bin frame mode) myocardial perfusion SPECT imaging was performed. During image acquisition breasts were fixated upwards in all female patients. Within 3 months before or after MPS study, diagnostic CA was made. Treadmill exercise or pharmacological stress by dipyridamol was used. GE Infinia and GE Millenium gamma camera systems were used for radionuclide imaging procedure. By means of cardiac quantitation program called 'Emory Cardiac Toolbox (ECTb)'; at the myocardial region reflecting the site of wall irregularity, nonstenotic plaque and coronary artery stenosis between 0-20% and 20-50% at coronary angiography were evaluated in respect to myocardial ischemia. All images were evaluated for attenuation artifacts. If reversible perfusion defects can not be explained by attenuation artifact, these were regarded as findings of myocardial ischemia<sup>8</sup>. Patients who have ischemic findings on SPECT images were called 'ischemic' and others were called 'nonischemic'. In all patients who have DM, HT or dyslipidemia, these diseases were documented and all of them had been using drug for various durations. 'Smoking positive' patients had been smoking any number of cigarette per day and for any duration. Exercise stress testing results were categorized as positive, negative or suspicious positive. Lesions were defined in LAD, Cx or RCA. left ventricular EF, mitral valve (MV) insufficiency

and left ventricular hypertrophy was evaluated by echocardiography. If present, ischemia on SPECT images was classified as mild, moderate or severe.

## Statistical analysis

'Independent samples t-test', in SPSS 11.5 program, to compare ages and BMI of ischemic and nonischemic patients; 'chi-square test', to compare distribution of gender, DM, HT, dyslipidemia, smoking, exercise stress testing results, effected coronary artery numbers, atherosclerotic lesion types, left ventricular EF, MV insufficiency and left ventricular hypertrophy in ischemic and nonischemic patients; 'Pearson's correlation coefficient test' or 'Spearman rank correlation test', to assess correlation between ischemia and the factors were used.  $P < 0.05$  was considered statistically significant.

## RESULTS

The study group comprised of 52 patients aged between 41-86 years (33 male, 19 female and mean age:  $57.1 \pm 10.4$  yrs). Body mass index (BMI) of patients ranged between 19.3 and 36.4 and mean  $\pm$  SD:  $28.1 \pm 4.2$ . There was no statistically significant difference between age and BMI of ischemic and nonischemic patients.

Clinical characteristics, coronary angiography and exercise stress testing results of the patients were shown on Table 1-3. Any of coronary arteries did not have more than one atherosclerotic lesion. At least one coronary artery territory of 22 of patients showed ischemic changes on MPS. Of them, 16 patients had history of at least one of the diseases that were hypertension, DM, dyslipidemia, cigarette smoking, MV insufficiency or left ventricular hypertrophy on echocardiography. However, 6 patients did not have any of cardiovascular risk factors and echocardiography findings were normal. Totally 126 coronary arteries were assessed. 83 of them were ischemic and 43 were normal on SPECT images. There was no statistically significant difference between the factors that may cause myocardial ischemia in ischemic and nonischemic patients (Table 1). In statistical analysis, poor significant correlation was found between ischemia and 2 factors that are BMI and gender whereas other factors did not show any significant correlation with ischemia ( $p > 0.05$ ). There was statistically poor correlation between atherosclerotic lesion stage and ischemia severity ( $p = 0.02$ ,  $r = 0.44$ ).

**Table 1.** Clinical, laboratory and demographic features of the patients and their statistical relationships with ischemia

Factors	Total	Ischemia (+)		Ischemia (-)		P
Gender						NS
Female	19	11	58%	8	42%	
Male	33	11	33%	22	67%	
Hypertension	24	8	33%	16	67%	NS
DM	9	2	22%	7	78%	NS
Dyslipidemia	13	4	31%	9	69%	NS
Smoking	22	7	32%	15	68%	NS
MV insufficiency (moderate or severe)	1	0	0%	1	100%	NS
LV hypertrophy	4	4	100%	0	0%	NS
Exercise stress testing						NS
Positive	11	6	55%	5	45%	
Suspicious	8	5	63%	3	37%	
Negative	12	5	42%	7	58%	
LVEF						NS
>50%	30	10	33%	20	67%	
30-50%	4	2	50%	2	50%	

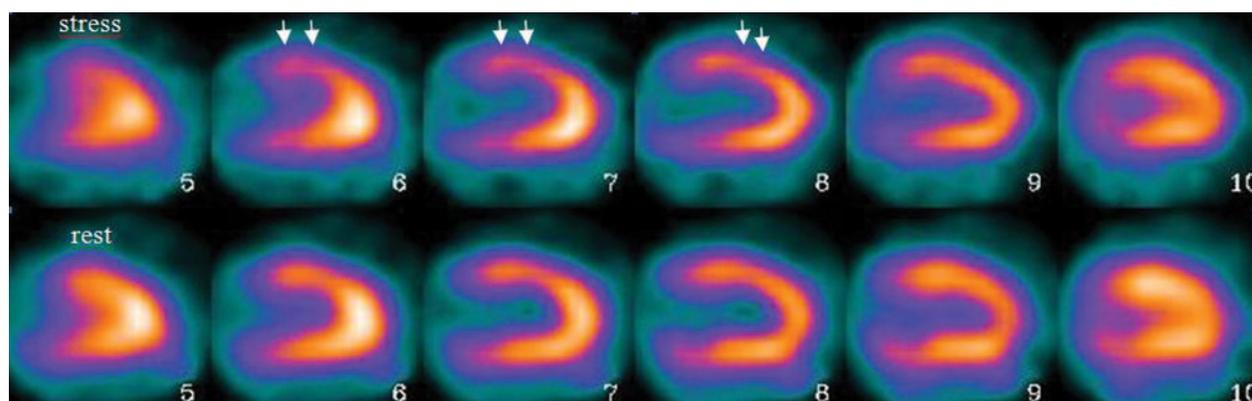
MV: Mitral valve, LV: Left ventricle, LVEF: Left ventricular ejection fraction, NS: Non significant ( $p>0.05$ )

**Table 2.** Coronary angiography and myocardial perfusion scintigraphy findings in 52 patients

Coronary artery lesions	No of coronary artery	Ischemia (+)		Ischemia severity			Ischemia (-)	
				Mild	Moderate	severe		
Normal	43	1	2%		1		42	98%
Wall irregularity	13	3	23%	3			10	77%
Nonstenotic plaque	24	7	30%	5	2		17	70%
Stenotic (0-20%)	29	10	34%	7	3		19	66%
Stenotic (20-50%)	17	7	41%	2	4	1	10	59%
Total	126	28	22%	17	10	1	98	78%

**Table 3.** Coronary arteries having atherosclerotic lesions and ischemia

Affected coronary arteries of patients	Total	Ischemia (+)		Ischemia (-)	
RCA	8	4	50%	4	50%
Cx	8	1	13%	7	87%
LAD	10	4	40%	6	60%
RCA and LAD	9	5	56%	4	44%
RCA and Cx	3	1	33%	2	67%
LAD and Cx	8	5	63%	3	37%
All	6	2	33%	4	67%
Total	52	22	42%	30	58%



**Figure 1.** SPECT images of 49 years old woman in whom coronary angiography revealed nonstenotic plaque in LAD. On vertical long axis SPECT images, reversible perfusion defects reflecting ischemia can be seen at anterior wall of the left ventricle (white arrows).

## DISCUSSION

The atherosclerotic coronary lesions such as wall irregularity, nonstenotic plaque and mild coronary artery stenosis are normally expected not to cause myocardial ischemia during exertion. However, in some patients with normal coronary anatomy on CA ischemic changes can be revealed on MPS.<sup>9</sup> Although many attenuation artifacts may cause such scintigraphic findings, not every case can be explained as artifact. In fact, many condition such as DM, HT, cardiomyopathies, syndrom X, dyslipidemia etc. may cause myocardial perfusion abnormalities due to endothelial or microvascular dysfunction.<sup>2,10-13</sup>

Many prior studies have emphasized the role of endothelial dysfunction as a potential cause of angina or abnormal functional results in patients with no significant documented CAD.<sup>14-20</sup> Rodés-Cabau et al.<sup>3</sup> have studied patients with angiographically mild coronary stenosis (<50% diameter stenosis by quantitative coronary angiography) by IVUS, fractional flow reserve (FFR) measurements and MPS. They have concluded that plaque burden as determined by IVUS might partly explain the presence of myocardial perfusion defects in cases of angiographically nonsignificant coronary lesions. However, the high FFR values associated with these lesions suggested that other mechanisms, such as endothelial/microvascular dysfunction, might also account for perfusion abnormalities in these patients. In this study, we assessed totally 52 patients having mild atherosclerotic lesions and detected ischemia in 22 of them on SPECT images. Most of ischemic

patients had some factors such as HT, DM, dyslipidemia, cigarette smoking, LV hypertrophy or MV insufficiency that may cause myocardial ischemia. But statistical analysis showed that there was no significant relationship between ischemia and these factors. Low subject number may contribute this result. Moreover, 6 ischemic patients didn't have any of them. No one in this group had a history of any other known disease. In these circumstances we couldn't explain ischemic changes by any reason other than endothelial dysfunction. Based upon this, we have thought that mild coronary atherosclerotic lesions can cause myocardial ischemia. But, we don't have any data that whether 'exercise-induced coronary spasm' that may cause myocardial ischemia was responsible for perfusion abnormalities at least in some of cases.

Verna et al.<sup>5</sup> have studied 20 patients referred for coronary angiography because of chest pain, abnormal exercise ECG, and abnormal myocardial perfusion findings. In that study, patients were evaluated by coronary anatomy and vasodilator capacity with IVUS and doppler flow velocity measurements. They concluded that reversible perfusion defects seen on 'single photon emission computed tomography' (SPECT) images are often associated with angiographically unrecognized occult atherosclerotic changes and an abnormal vasodilatation capacity of the coronary circulation. In our study, totally 83 coronary arteries (LAD, LCX or RCA) were evaluated and territories of 27 of them were found to be ischemic on MPS. We noticed that 17 of them (63%) were mildly, 9 (33%) were moderately

and only 1 (4%) was severely ischemic. We found statistically poor correlation between lesion stage and ischemia severity ( $p=0.02$ ,  $r=0.44$ ). Mild ischemic findings on SPECT images may be deemed to be suspicious by some physicians, so ones may not report some scintigraphically mild ischemic findings to increase specificity of the procedure. Thus, the test results may vary from centers to centers.

A limitation of this study is that the myocardial ischemia caused by atherosclerotic lesions can be detected more accurately by PET imaging than MPS.<sup>21</sup> Moreover; we didn't perform fractional flow reserve or doppler flow velocity measurements or any other test that evaluates endothelial/microvascular dysfunction to confirm MPS findings. We also didn't do any other anatomical imaging techniques such as IVUS for coronary anatomy other than angiography.

In conclusion, based upon the study findings, we suggest that insignificant atherosclerotic lesions (<50%) even at very early stages may cause myocardial ischemia in some of patients that can be detected easily by myocardial perfusion scintigraphy. Therefore, therapeutic intervention can be thought for this kind of the patients in case of having ischemic findings on MPS.

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