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Tc-99m MIBI myocard perfusion SPECT findings in patients with typical chest pain and normal coronary arteries

Tipik göğüs ağrısına karşın koroner arterleri normal olan olgularda Tc-99m MIBI myokard perfüzyon sintigrafisi bulguları

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Summary

Aim: The aim of this study was to determine the regional distribution of myocardial perfusion abnormalities and defect size using Tc-99m MIBI myocardial perfusion scintigraphy (MPS) in patients with anginal chest pain, positive exercise test and angiographically normal coronary arteries.

Material and Methods: Eighty-one (81) patients (40 male, 41 female) who have angina pectoris, positive stress ECG and normal coronary angiography were included this study. Clinical data of these patients who underwent Tc-99m MIBI MPS were retrospectively reviewed. For MPS imaging, the two-day stress-rest Tc-99m MIBI protocol was used. SPECT data were evaluated both visually and semi-quantitatively. The number of abnormal segments was defined as the defect number (DN).

Results: There were 65 (80.3%) patients with abnormal MPS and all of these perfusion abnormalities were reversible defects. Frequency of smoking, hyperlipidemia and diabetes mellitus was significantly higher in patients with abnormal MPS than normal MPS. The proportion of postmenopausal women was also higher in the MPS positive group. Most of the myocardial perfusion defects were seen on the nferior wall in both male and female patients on MPS images. The difference between the mean values of DN in the diabetic and nondiabetic groups was statistically significant (5.66±3.14 and 4.51±2.90 respectively. p=0.041).

Conclusion: A high prevalence of myocardial perfusion defects was observed in our patients with syndrome X. All of these perfusion abnormalities were reversible. We conclude that the presence of perfusion defects on MPS is a significant objective indicator in patients with cardiac syndrome X.

Key words: Cardiac syndrome X, myocard perfusion SPECT, Tc-99m MIBI.

Özet

Amaç: *Bu çalışmada anjinal göğüs ağrısı olan, eforlu EKG testi pozitif ve koroner anjiyografide anlamlı stenoz saptanmayan olgularda myokard perfüzyon sintigrafisi bulgularını değerlendirmek amaçlandı.*

Yöntem ve Gereç:*Göğüs ağrısı olan, eforlu EKG'si pozitif ve koroner anjiyografisi normal 81 (41 kadın, 40 erkek) olguya ait Tc-99m MIBI myokard perfüzyon sintigrafisi (MPS) bulguları retrospektif olarak incelendi. Tüm olguların eforlu EKG, ekokardiyografi ve anjiyografisi mevcuttu. MPS vizüel ve semikantitatif yöntemle incelendi. MPS bulguları ile olguların klinik özellikleri ve diğer kardiyolojik test sonuçları arasındaki arasındaki korelasyon değerlendirildi.*

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Bulgular:*Atmışbeş olguda (% 80.3) MPS'de reversibl perfüzyon defektleri saptandı. Olguların hiçbirinde fiks perfüzyon defekti gözlenmedi. Hiperlipidemi, sigara kullanımı, diabetes mellitus sıklığı ve postmenapozsal dönemdeki kadın oranı MPS'de perfüzyon defekti saptanan olgularda normal olanlardan daha yüksekti. Semikantitatif incelemede MPS'de 81 hastada toplam 1620 segmentten 401'inde (% 24.8) perfüzyon defekti izlendi. Her iki cinstede en sık inferior duvarda perfüzyon anomalisi gözlendi. Diabetik olgularda defekt sayısının anlamlı biçimde daha yüksek olduğu dikkat çekti (sırasıyla; 5.66±3.14 ve 4.51±2.90, p=0.041).*

Sonuç:*Sendrom X'li olgularda MPS ile saptanan myokardiyal perfüzyon defekti sıklığının yüksek ve bu perfüzyon anomalilerinin tümünün iskemi ile uyumlu karakterde olduğu saptandı. Kardiyak sendrom X'li olgularda MPS'nin perfüzyon anomalilerinin varlığını değerlendirmede önemli bir objektif gösterge olduğu sonucuna varıldı.*

Anahtar kelimeler: *Kardiyak sendrom X, myokard perfüzyon sintigrafisi, Tc-99m MIBI.*

Introduction

The term cardiac syndrome X is used to describe patients with anginal chest pain, a positive exercise test and a normal coronary angiography (1). There has been no specific cause or single pathophysiological mechanism that could clarify this syndrome. It has been reported that increased sympathetic tone (2,3) or endothelial dysfunction that led to increased vasoconstrictor tone of pre-arteriolar vessels (4) and abnormal myocardial blood flow distribution (5) may be responsible for the disease. Endothelial dysfunction is likely to be multifactorial in these patients and possible risk factors such as diabetes mellitus, smoking, obesity, hypertension and hyperlipidemia can contribute to its development. Estrogen deficiency and postmenopausal state has also been proposed the pathogenesis of this disease in female patients (6). Some patients demonstrated rest or stress electrocardiographic changes. Some of these had regional perfusion defects indicated by myocardial ischemia on stress myocardial perfusion scintigraphy (6-10).

The aim of this study was to determine the regional distribution of myocardial perfusion abnormalities and defect size using Tc-99m MIBI myocardial perfusion single photon emission computed tomography (SPECT) and echocardiography in patients with anginal chest pain, positive exercise test and angiographically normal coronary arteries. In the current study we also evaluated the relation with risk factors such as diabetes mellitus, hyperlipidemia, smoking, hypertension and other clinical findings.

Materials and Methods

Patients:

Clinical data of patients who were referred our clinic for Tc-99m MIBI myocardial perfusion scintigraphy (MPS) between 2005 and 2007 were retrospectively reviewed. Eighty-one (81) patients who had typical angina pectoris, positive stress ECG were referred for myocardial scintigraphy, however all patients had normal coronary angiography. All of these patients had basal ECG and rest echocardiography and they were evaluated for cardiac risk factors like hypercholesterolemia, hypertension and diabetes mellitus. The mean age was 55.2±7.05. In our study group there were 40 male (mean age: 55.3±7.03) and 41 female (mean age: 55.2±7.16) patients. Patients with valvular heart disease, global LV hypertrophy, complete brandle branch block and myocardial disease detected by echocardiography were excluded from the study. Informed consent was obtained in all patients.

Basal and Exercise stress ECG; A 12-lead electrocardiogram was obtained at rest. *Exercise stress ECG;* was applied on a treadmill under a standard Bruce protocol. The exercise test was considered positive if there was a horizontal or down sloping ST segment depression of larger than 1 mm for 80 microseconds after the J point.

Echocardiography; was obtained using standard techniques. Mean values of consecutive 3 cardiac cycles were evaluated in echocardiographic measures. Myocardial wall and valvular motions were investigated on M-mode study.

Coronary angiography**;** was performed using the Seldinger technique, within 3 weeks of scintigraphic imaging in all patients. Multiple orthogonal projections were obtained. A normal coronary angiogram was defined as insignificant (≤50%) coronary artery stenosis. However, there were no patients with ≥ 30% coronary stenosis in our study group.

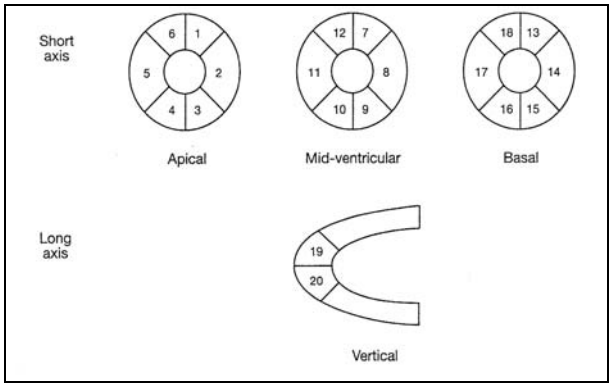
Tc-99m MIBI Myocardial Perfusion SPECT Imaging:

Two-day stress-rest Tc-99m MIBI protocol was used. All cardiovascular medications were discontinued 72 hours prior to the study. All patients underwent an exercise treadmill stress test according to the modified Bruce protocol for stress MPS imaging. Exercise termination

criteria were: achievement of maximal age-related heart-rate (220 beats per min – age), ≤ 2 mm ST segment depression, severe angina or cardiac rhythm abnormalities, physical exhaustion. At near maximal exercise 20 mCi (740 MBq) of Tc-99m MIBI was given intravenously and exercise continued following 2 minutes. Rest images were obtained after 3 hour's rest with 20 mCi Tc-99m MIBI. Stress and rest data were gathered using a dual headed (Sophy DST) gamma camera equipped with low energy, all purpose collimators at 45 minutes after radiopharmaceuticals injection. Thirty-two projection images of 64x64 matrixes were obtained at a rate of 40 seconds per image over an 180º arc, extending from the 45º right anterior oblique to the 45º left posterior oblique projections for all SPECT data.

Data interpretation: SPECT data were evaluated both visually and semi-quantitatively. On visual assessment, regional perfusion abnormality and defect reversibility was noted. For the semi-quantitative analysis, a model of 20 myocardial segments was formed by using apical, mid-ventricular, basal short axis and vertical long axis images (Figure-1). Each segment was classified using colour scale as normal or abnormal (lower than 50% of the highest count activity). The number of abnormal segments was determined for each patient and defined as the defect number (DN). Combining both stress and rest images, reversibility was defined as an improvement of at least 25% of tracer uptake on subsequent images. A perfusion abnormality on the stress image showing partial or complete normalization on the rest image was designated as a reversible abnormality or ischemia. There were no patients with fixed perfusion defects in our study group.

Figure 1: A model of 20 segments formed by using apical, mid-ventricular and basal short axis vertical long axis images is shown.



The patients were divided into two groups as normal and pathological according to myocard perfusion scintigraphy findings.

The segments in each slice were allocated to coronary artery territories. The anterior wall, septum and apex were assigned to the left anterior descending (LAD) artery territory. Segments covering the inferior wall were assigned to the right anterior descending (RCA) artery territory. The lateral wall was assigned to the left circumflex (LCX) artery territory.

Statistical Analysis:

All values are expressed as mean value ± standard deviation. The statistical analysis was performed using SPSS software (version 11.0, SPSS Inc, USA). Unpaired Student t test was used to analyize comparisons between groups. A p value ≤ 0.05 was considered statistically significant.

Results

Patients:

Clinical characteristics of 81 patients are presented in (Table-1). There were 65 (80.3%) patients with abnormal MPS and all of these perfusion abnormalities were reversible defects. Frequency of smoking, hyperlipidemia and diabetes mellitus was significantly higher in patients with abnormal MPS than in those with normal MPS.

Basal (Rest) ECG:

Non-specific changes such as ST segment and T wave abnormalities at basal ECG were observed in 37 patients. Of these patients, 33 had reversible perfusion defects in MPS and four patients had normal Tc-99m MIBI SPECT. The location of perfusion defects in MPS and abnormality observed in ECG was concordant in 29 patients. Non-ischemic findings such as rhythm abnormalities were determined in 15 cases. The remaining 29 patients had normal rest ECG (27 of these were MPS positive). Accordance with MPS and rest ECG was 69% (56 patients) in all study groups.

Stress ECG: Ischemic findings were detected by exercise stress ECG in all patients.

Rest Echocardiography:

Sixty of 81 patients (74%) had completely normal rest echocardiography. Of these patients with normal echocardiography, 8 had normal and the remaining 52 had abnormal MPS findings. Diastolic dysfunction and septal hypertrophy of the left ventricle were observed in 4 (5%) patients. Myocardial hypokinesia was determined on various segments in 17 (21%) patients in whom reversible perfusion defects were observed in MPS.

Table 1: Clinical characteristics and cardiologic test results of patients with anginal chest pain, positive exercise ECG and normal coronary angiogram.

	MPS positive	MPS negative	p
Total number of patients	65 (80.3%)	16 (19.7%)	**
Women/ Men	32 / 33	9 / 7	p>0.05
Mean Age (years)	55.2±7.05	55.3±6.88	p>0.05
Postmenopausal women	31 / 65 (47%)	5 (31%)	p<0.05*
Smoking	24 / 65 (37%)	3 / 16 (19%)	p<0.05*
Hypertension	33 / 65 (51%)	8 / 16 (50%)	p>0.05
Hyperlipidemia	37 / 65 (57%)	7 / 16 (44%)	p<0.05*
Diabetes mellitus	22 / 65 (34%)	0	p<0.05*
Obesity	49 / 65 (75%)	11 / 16 (69%)	p>0.05
Ischemic basal ECG Findings	33 / 65 (51%)	4 / 16 (25%)	p<0.05*
Echocardiographic abnormality	19 / 65 (29%)	1 / 16 (6%)	p<0.05*

Unpaired Student t test

Tc-99m MIBI Myocardial Perfusion Scintigraphy:

In our series, myocardial perfusion SPECT imaging was normal in 16 (19.7%) and abnormal in 65 (80.3%) patients. All of the perfusion defects detected by MPS were reversible. A total of 1620 segments were analyzed using semi-quantitative visual analysis in 81 patients. One thousand two hundred and nineteen (1219) of these segments were normal (75.2%). Reversible perfusion defects were observed in the remaining 401 segments (24.8%) in a total of 65 patients. Most of the myocardial perfusion defects were seen on the inferior wall in both male and female patients. Second mostly observed perfusion defects in women were anterior wall and septum while in men, apex and anterior wall defects were more prominent. Regional distribution of perfusion defects was as follows: inferior wall in 35 patients (13 female, 22 male), anterior wall in 27 (11 female, 6 male), septum in 14 (11 female, 3 male), apex in 11 (4 female, 7 male) and lateral wall in 7 patients (3 female, 4 male) (Figure-2). The location and extent of perfusion defects are presented in (Table-2). Myocardial perfusion defects were in single coronary vascular territory in 45 patients (69%) and two vascular territories in 20 patients (31%). There were no perfusion abnormalities leading to three coronary vascular territories.

In the current study we also evaluated the extent of perfusion abnormalities described as the number of perfusion defects (DN=Defect Number). All of these perfusion defects were reversible. The mean DN was 4.80±3.44 in the whole study population. Relation between cardiac risk factors, sex and mean DN are shown in (Table-3). The difference between the mean values of DN in diabetic and nondiabetic groups was statistically significant (5.66±3.14 and 4.51±2.90 respectively. p= 0.041).

Table-2. Number and location of perfusion defects. **DN=Defect Number:** Number of segments defined as reversible in MPS according to a myocardial model. **n=** number of patients. **Single regional perfusion defects:** Perfusion defects located on single myocardial wall or region. **Multiregional perfusion defects:** Perfusion defects located on two or more myocardial wall and regions (regardless of one or two coronary artery territories).

Location	Number of pts with perfusion defects	Female/ male	Single- regional (n)	Multi- regional (n)	Total DN
Anterior	27 (41.5%)	11/16	12	15	134
Inferior	35 (53.8%)	13/22	22	13	182
Septum	14 (21.5%)	11/3	5	9	42
Apex	11 (16.9%)	4/7	1	10	22
Lateral	7 (10.7%)	3/4	2	5	21

Figure 2: Percentage of reversible perfusion defects in MPS according to their location.

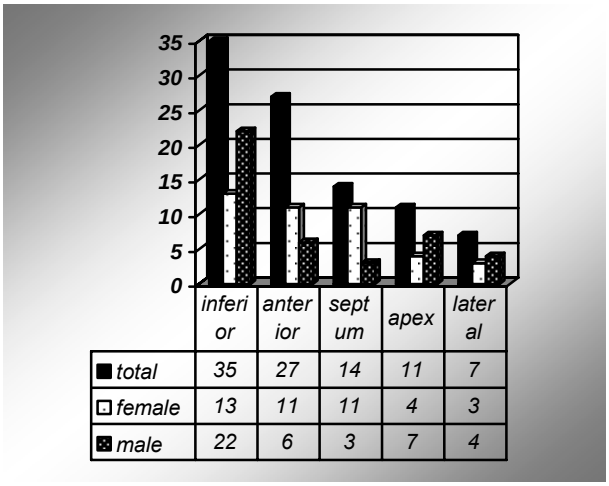


Table 3: Clinical parameters and mean defect number of patients with syndrome X.

Characteristics	Mean DN	p
Male	4.76±3.46	0.98
Female	4.75±3.36	
Smoking (+)	4.80±3.37	1.03
Smoking (-)	4.80±3.44	
Hypertension (+)	4.86±3.44	0.72
Hypertension (-)	4.80±3.43	
Hyperlipidemia (+)	4.77±3.34	0.52
Hyperlipidemia (-)	4.78±3.46	
Diabetes mellitus (+)	5.66±3.14	0.041**
Diabetes mellitus (-)	4.51±2.90	
Obesity (+)	4.64±2.92	0.12
Obesity (-)	4.53±3.22	

Unpaired Student t Test

Discussion

A sizeable proportion (20- 30%) of patients with anginal chest pain and positive exercise test have normal or near normal coronary arteries (11). These patients were determined to have syndrome X and a high prevalence of myocardial perfusion defects were also observed in this patient population (6-16). When the reported literature was reviewed, the percentage of perfusion abnormalities was variable as, 72% (8), 62.7% (9), 40% (10), 70% (15) and 89% (16). Some studies noted that all of the perfusion abnormalities were reversible (7,10,12), while fixed perfusion defects were also reported in other series (8,913-15). In our study, MPS was abnormal in 65 (80.3%) patients. All of the perfusion defects detected by MPS were reversible so that our values were slightly higher than some of the studies (8,9,10,15). These differences can be explained by the inclusion criteria of patient data, since some groups included all patients with negative as well as positive stress ECG. The correlation between positive stress ECG and abnormal myocardial perfusion scintigraphy has not been settled in patients with syndrome X. Although a study reported that the probability of myocardial perfusion defects in MPS was significantly higher in patients with positive stress ECG, conflicting reports were also published (8,10,15,16). The main difference of our study with respect to other groups is that our study population only consisted of patients who had typical anginal chest pain and a positive stress test. Therefore, the probability of myocardial ischemia was relatively higher.

The issue of whether abnormal MPS findings should represent true perfusion abnormalities or may be interpreted as false-positive remains controversial in patients with angiographically normal coronary arteries. When Thallium-201 (Tl-201) is used as a myocardial perfusion imaging agent, the attenuation problems due to the soft tissues (such as breast or diaphragm) are not uncommon because of its low physical-energy emission. On the other hand, Tc-99m MIBI is a myocardial agent with a higher energy emission and higher imaging characteristics than Tl-201. Its technical properties have been introduced to attempt to reduce the frequency of artifactual defects (17). Therefore in our series Tc-99m MIBI was preferred in order to minimize the possibility of false positive reports.

In patients with normal coronary arteries, the physiopathologic mechanisms leading to myocardial perfusion abnormalities have been discussed. Verna E. et al, studied syndrome X patients with intracoronary sonography and reported that, angiographically occult atherosclerotic changes such as noncalcific plaques, abnormal vasodilatation capacity and low coronary flow reserve could lead to the myocardial perfusion defects on MPS (18). It has been suggested that, increased sympathetic tone (2,3), endothelial dysfunction (4) and abnormal myocardial blood flow distribution might also be responsible for these perfusion abnormalities (5). Additionally, some authors reported that syndrome X was a systemic disorder so that the prevalence of brain perfusion abnormalities on brain SPECT was high (19). The brachial artery flow of patients who had positive MPS was also low (20).

When the clinical characteristics and cardiac risk factors of 81 patients in our study were evaluated, the percentage of the smoking, hyperlipidemia and diabetes

mellitus were significantly higher in patients with abnormal MPS than in those with normal MPS (37% vs 19%; 57% vs 44% and 34% vs. 0% respectively) (Table-1). Studies that investigated the clinical parameters of syndrome X patients who had positive MPS findings with respect to normal control subjects found no significant clinical characteristic difference (7,14). However, Kaski et al. noted that the microvasculary dysfunction was multifactorial and a number of risk factors such as hypertension, hypercholesterolemia, diabetes mellitus and smoking could contribute to development of this disease (6).

In this study, we also correlated the cardiologic tests such as basal ECG and rest echocardiography with MPS. The main limitation of our study was the lack of Gated analysis application. Gated analysis would help to evaluate left ventricular contractile function. This limitation was overcome by using the parameters of echocardiography.

Both the frequency of non-specific findings in basal ECG and myocardial wall motion abnormalities detected by echocardiography were significantly higher in MPS positive group than patients with normal MPS (Table-1). All patients in our study group had positive a exercise test, therefore the relation between MPS and exercise ECG findings was not examined. Reversible perfusion defects were detected in all segments corresponding to myocardial dysfunction on echocardiography. However, regional myocardial dysfunction in rest echocardiography is not a common finding in patients with syndrome X who had ischemic results in a myocard perfusion scan. Therefore, those echocardiography abnormalities should be interpreted with caution. Dobutamine stress echocardiography might also give additional information and a number of authors suggested the use of dobutamine stress echocardiography in patients with syndrome X especially those who had perfusion defects on MPS (21,22). Fragasso et al. reported that there were regional left ventricle wall motion abnormalities during stress echocardiography in more than half of the syndrome X patients with positive MPS (22). However, conflicting results were also reported so that dobutamine stress echocardiography was found as insensitive for ischemia caused by micro vascular dysfunction (13).

When the regional distribution of myocardial perfusion defects was analyzed, the majority of the patients, both male and female, had inferior wall abnormalities. The second most observed perfusion defects in women were anterior wall and septum while in men apex and anterior wall defects were more prominent (Table-2, Figure-2). Tc-99m MIBI is a preferred myocardial perfusion agent with higher energy emission and better image characteristics to reduce the frequency of false positive results due to attenuation and artifactual defects. The observation of similar perfusion defects in both sexes, inferior and anterior walls, led us to assume that the possibility of false positive results in our series was low. Several investigators have also supported this finding since, the majority of perfusion defects were observed in inferior and anterior walls (7,8,15). Furthermore, Hsu et al. and Çavuşoğlu et al. studied a group of healthy controls that had no clinical symptoms and findings (7,8). Both groups observed that control groups did not have a significant myocardial perfusion abnormality; therefore they concluded that the perfusion defects diagnosed in syndrome X patients might not be artefactual.

In our study group, myocardial perfusion defects were diagnosed at single coronary vascular territory in 45 patients (69%) and two vascular territories in 20 patients (31%). There were no perfusion abnormalities leading to three coronary vascular territories. The extent of perfusion defects was defined as the number of segmental perfusion defects (DN=Defect Number). The mean DN was 4.80±3.44 in patients with positive MPS. When the mean DN values were compared, the difference between diabetic and non-diabetic groups was statistically significant (5.66±3.14 and 4.51±2.90, respectively) ($p= 0.041$). There was no significant correlation between gender, smoking, and presence of hypertension, hyperlipidemia and obesity with the extent of perfusion defects. A recent study has indicated that multiregional perfusion defects corresponding to multiple vascular territories in patients with syndrome X might be an indicator of a diffuse process of micro vascular disease (7,23,24). On the other hand, the prognostic roles of multiregional perfusion defects have not been clearly identified in syndrome X. Our study was not designed to assess the prognostic implications of MPS findings. However, Sun et al. reported that more patients developed cardiomegaly in the group with abnormal MPS than patients with normal MPS in cardiac syndrome X, while both groups were at low risk for cardiac events such as cardiac death or myocardial infarction (9). In their study, 9 of 33 patients with positive MPS developed cardiomegaly and left ventricular dysfunction during 10 years of follow-up. They concluded that the presence of a perfusion defect on MPS was an important factor contributing to the impairment of left ventricular function and that it was possible to identify a subgroup of patients at high risk of developing left ventricular dysfunction and cardiomegaly over years in cardiac syndrome X (9).

Conclusion

A high prevalence of myocardial perfusion defects on Tc-99m MIBI MPS was observed in our patients with syndrome X. All of these perfusion abnormalities were reversible and tended to be at single vascular territory. The extent of perfusion defects was higher in some groups of patients with diabetes mellitus. We conclude that the presence of perfusion defects on MPS is a significant objective indicator in patients with cardiac syndrome X. However, further studies that investigate prognostic importance of perfusion abnormalities will be required.

Kaynaklar

1. Kemp HG Jr. Left ventricular function in patients with anginal syndrome with normal coronary arteriograms. Am J Cardiol 1973; 32: 375-376.
2. Montorsi P, Fabbiocchi F, Loaldi A, et al. Coronary adrenergic hyperreactivity in patients with syndrome X and abnormal electrocardiogram at rest. Am J Cardiol 1991; 68: 1698-1703.
3. Rosano GMC, Ponikowski P, Adamopoulos S, et al. Abnormal autonomic control of the cardiovascular system in syndrome X. Am J Cardiol 1994; 73: 1174-1179.
4. Quyyumi AA, Cannon RO, Panza JA, Diodati JG, Epstain SA. Endothelial dysfunction in patients with chest pain and normal coronary arteries. Circulation 1992; 86: 1864-1871.
5. Shirashi A, Ikeda H, Haramaki N, et al. Abnormal myocardial blood flow distribution in patients with angina pectoris and normal coronary arteriograms. Jpn Circ J 2000; 64: 566-571.
6. Kaski JC, Aldama G, Cosin-Sales J. Cardiac syndrome X. Diagnosis, pathogenesis and management. Am J Cardiovasc Drugs 2004; 4: 179-194.
7. Cavuşoğlu Y, Entok E, Timuralp B et al. Regional distribution and extent of perfusion abnormalities, and lung to heart uptake ratios during exercise thallium-201 SPECT imaging in patients with cardiac syndrome X. Can J Cardiol 2005; 21: 57-62.
8. Hsu HB, Shiau YC, Kao A et al. Technetium-99m tetrofosmin myocardial perfusion single photon emission computed tomography in syndrome X. A preliminary report. Jpn Heart J 2003; 44: 153-162.
9. Sun SS, Huang JL, Tsai SC, Ho YJ, Kao CH. The higher likelihood of developing cardiomegaly during follow-up in patients with syndrome X and abnormal thalium-201 myocardial perfusion SPECT. Int J Cardiovasc Imaging 2001; 17: 271-278.
10. Kao CH, Wang SJ, Ting CT, Chen YT. Tc-99m sestamibi myocardial SPECT in syndrome X. Clin Nucl Med 1996; 21: 280-283.
11. Sullivan AK, Holdright DR, Wright CA, et al. Characterisation and follow-up of patients with chest pain and normal coronary arteries. J Am Coll Cardiol 1993; 121: 317A.
12. Fujita H, Yamabe H, Yokoyama M. Dipyridamole-induced reversible thallium-201 defect in patiens with vasospastic angina and nearly normal coronary arteries. Clin Cardiol 2000; 23: 24-30.
13. Zouridakis EG, Cox ID, Garcia-Moll X at al. Negative stress echocardiographic responses in normotensive and hypertensive patients with angina pectoris, positive exercise stress testing, and normal coronary arteriograms. Heart 2000; 83: 141-146.
14. Lorenzo AD, Lima RSL, Siqueira-Filho AG, Pantoja MR. Prevalence and prognostic value of perfusion defects detected by stress technetium-99m sestamibi myocardial perfusion single-photon emission computed tomography in asymptomatic patients with diabetes mellitus and no known coronary artery disease. Am J Cardiol 2002; 90: 827-832.
15. Ortega A, Moreno R, Alonso JC et al. Results of myocardial scintigraphy with 99mTc-tetrofosmin and dipyridamole administration in patients diagnosed of microvascular angina. Rev Esp Med Nucl 2000; 19: 337-73.
16. Kao CH, Wang SJ, Ting CT, Chen YT. Thallium-201 myocardial SPET in strictly defined syndrome X. Nucl Med Commun 1995; 16: 640-6.
17. Taillefer R, Lambert R, Essiambre R et al. Comparison between thallium-201, technetium-99m sestamibi and technetium-99m teboroxime planar myocardial perfusion imaging in the detection of coronary artery disease. J Nucl Med 1992; 33: 1091-98.
18. Verna E, Ceriani L, Giovanella L et al. 'False-positive' myocardial perfusion scintigraphy findings in patients with angiographically normal coronary arteries : Insights from intravascular sonography studies. J Nucl Med 2000; 41:1935-40.
19. Pai PY, Liu FY, Kao A, Lin CC, Lee CC. A higher prevalence of abnormal regional cerebral blood flow in patients with syndrome X and abnormal myocardial perfusion. Jpn Heart J 2003; 44: 145-152.

20. Masci PG, Laclaustra M, Lara JG, Kaski JC. Brachial artery flow-mediated dilation and myocardial perfusion in patients with cardiac syndrome X. Am J Cardiol 2005; 95: 1478-80.
21. Plance E, Alberzoni A, Fea F, Colombo G. Usefulness of stress echocardiography in the diagnosis of syndrome X. Cardiologia 1998; 43: 839-46.
22. Fragasso F, Chierchia SL, Lu C et al. Left ventricular dysfunction during dobutamine stress echocardiography in patients with syndrome X and positive myocardial perfusion scintigraphy. G Ital Cradiol 1999; 29: 383-90.
23. Delcour KS, Khaja A, Chockalingam A, Kuppuswamy S, Dresser T. Outcomes in patients with abnormal myocardial perfusion imaging and normal coronary angiogram. Angiology 2009;60:318-21.
24. Fragasso G, Chierchia SL, Arioli F, Carandente O, Gerosa S, Carlino M, Palloshi A, Gianolli L, Calori G, Fazio F, Margonato A. Coronary slow-flow causing transient myocardial hypoperfusion in patients with cardiac syndrome X: Long-term clinical and functional prognosis. Int J Cardiol 2009;137:137-44.