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Characteristics of Patients with Abnormal Stress Technetium Tc 99m Sestamibi SPECT Studies without Significant Coronary Artery Diameter Stenoses

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Summary

Background: Single-photon emission computed tomography (SPECT) sestamibi (MIBI) is an excellent tool for detection of coronary artery disease (CAD), preoperative risk assessment, and follow-up management after coronary revascularization. While the sensitivity of MIBI SPECT for detecting CAD has been reported to exceed 90%, the specificity ranges between 53–100%.

Hypothesis: The study was undertaken to assess characteristics of patients with abnormal stress technetium Tc 99m sestamibi SPECT (MIBI) studies without significant coronary artery diameter stenoses (< 50%).

Methods: Between January 1999 and November 2000, 270 consecutive patients were referred for coronary angiography due to reversible MIBI uptake defects during exercise. In 41 patients (15%; 39% women, mean age 59 ± 9 years), reversible MIBI uptake defects were assessed although coronary angiography showed no significant CAD. These patients were compared with age- and gender-matched patients with perfusion abnormalities (39% women, mean age 60 ± 9 years), due to significant CAD (coronary artery stenosis > 50%).

Results: There were no significant differences between the two groups regarding body mass index, left bundle-branch block (LBBB), or method of stress test (dipyridamole in patients with LBBB or physical inactivity [n = 11] and exercise in all the others [n = 30]). Left ventricular hypertrophy (44 vs. 23%, p = 0.05) and left anterior fascicular block (LAFB) (17 vs. 0%, p = 0.005) were more common in patients with perfusion abnormalities with no significant CAD, whereas ST-segment depression during exercise (17 vs. 37% p = 0.05) and angina during exercise (15 vs. 29%, p = 0.02) were significantly less common than in patients with abnormal MIBI perfusion studies and angiographically significant CAD. Sestamibi uptake defects during exercise were significantly smaller in patients without significant CAD than in matched controls with significant CAD (p < 0.0004).

Conclusion: Of 270 consecutive patients, 41 (15%) referred to coronary angiography due to reversible MIBI uptake defects showed coronary artery stenoses < 50%. Twenty-six (10%) of these presented angiographically normal coronary arteries. The significantly higher proportion of left ventricular hypertrophy and LAFB in patients with reversible MIBI uptake defects without significant CAD suggest microvascular disease, angiographically underestimated CAD, and conduction abnormalities as underlying mechanisms.

Key words: single-photon emission computed tomography sestamibi, coronary artery disease, left ventricular hypertrophy, left bundle-branch block

Introduction

Single-photon emission computed tomography (SPECT) sestamibi (MIBI) is an excellent tool for detection of coronary artery disease (CAD), preoperative risk assessment, and follow-up management after coronary revascularization. While the sensitivity of MIBI SPECT for detecting CAD has been reported to exceed 90%, the specificity ranges between 53–100%.[1] A referral bias of invasive work-up of patients with positive MIBI SPECT only and microvascular disease has been one of the reported reasons for the relatively wide range of specificity.[1–3] This study assessed the characteristics

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of patients with angiographically normal coronary arteries and abnormal MIBI SPECT scans and compared them with an age- and gender-matched group with perfusion abnormalities due to angiographically significant coronary artery diameter stenoses.

Methods

Patients and Materials

Between January 1999 and November 2000, 1,000 consecutive MIBI SPECT studies were performed. A stress test was either obtained on a bicycle ergometer with a peak heart rate > 80% of the age-predicted value (215 beats/min − age) or with intravenous dipyridamole (0.56 mg/kg/min for 4 min) if an exercise stress test could not be performed (e.g., because of knee or hip problems) and in all patients with left bundle-branch block (LBBB). In all, 270 (27%) patients were referred to coronary angiography due to reversible MIBI uptake defects. Of these, 41 had abnormal MIBI scans and no significant CAD (stenosis < 50%) and were compared with 41 age- and gender-matched controls with perfusion abnormalities in MIBI scans and significant CAD (stenosis > 50%).

Technetium 99m MIBI SPECT

All patients received an intravenous dose of ^{Tc99m}MIBI (15 mCi) 60 s before the end of exercise. The same dose was used for the study at rest. Stress and rest studies were performed on two consecutive days. Images were acquired 1 h after administration of ^{Tc99m}MIBI using a Picker® gammacamera Prism 2000 XP (Picker International Nuclear Medicine Division, Cleveland, Ohio, USA), equipped with a low-energy high-resolution collimator and a semicircular orbit of 180˚, starting at 30˚ right anterior oblique and detections every 3˚. Reconstruction was performed by filtered backprojection using a low pass filter. Short axis, horizontal long axis, and vertical long axis were obtained according to current recommendations.[4] Twenty segments were evaluated qualitatively by consensus of at least two experienced observers, and the uptake in each of these segments was assessed as normal, mild (= equivocal), moderate, severe, or absent.[5] In addition, a polar plot model of the left ventricular (LV) wall was used for semiquantitative analysis to describe the extent and severity of the perfusion defects using Cequal® computer analysis (Picker). History of chest pain and ST-segment analysis of the 41 patients with abnormal perfusion scans were obtained by reviewing their medical reports. Left ventricular hypertrophy was assessed echocardiographically using the cube formula with correction of overestimation by the equation proposed by Devereux *et al.*[6] An LV muscular mass index > 114 g/m^2 in women and > 135 g/m^2 in men was defined as LV hypertrophy.

An age- and gender-matched control group with abnormal MIBI scans and significant CAD was assessed on a consecutive basis to compare their clinical data with the study group.

Statistics

All data are expressed in numbers and percentages or in frequencies and means (± standard deviation) where appropriate. The chi-square test was used to compare results between the two groups.

Results

In all, 1,000 MIBI SPECT scans were performed from January 1999 to November 2000. Of these, 730 (73%) scans were normal (i.e., no reversible MIBI uptake defects) and no further examinations were performed in these patients. The remaining 270 (27%) patients were referred to coronary angiography due to predominantly reversible (49%) or fixed and reversible (51%) MIBI uptake defects during exercise. In 41 (15%) (39% women, mean age 59 ± 9 years), significant CAD (stenosis < 50%) could be excluded angiographically and in 26 (10%) of these patients normal coronary arteries were found. Baseline clinical characteristics (Table I) were compared with an age- and gender-matched control group (60 ± 9 years) with reversible stress defects due to significant CAD on angiography. There were no significant differences between the two groups considering body mass index, kind of exercise (dipyridamole vs. physical stress) and LBBB. Hypertension (49 vs. 27% p = 0.04), LV hypertrophy (18 vs. 9%; p = 0.05), and left anterior fascicular block (LAFB) (17 vs. 0%; p = 0.005) were significantly more common in patients without significant CAD. Hyperlipidemia (66 vs. 32% p = 0.002) was more common in patients with CAD. Left ventricular hypertrophy was found in four of seven patients (57%) showing LAFB. The uptake defects in patients with LAFB were located in the basal septal segment in three cases, the inferobasal segment in three cases, and the anteroapical segment in one case. Significantly more fixed MIBI uptake defects were found in patients with significant CAD than in the study group (Table II). Angina (29 vs. 15%; p = 0.02) and ST-segment depression on electrocardiogram (ECG) (37 vs. 17%; p = 0.05) during physical or pharmacologic stress test were significantly more common in patients with CAD. Patients with "false-positive" MIBI scans had significantly more mild and moderate MIBI uptake defects during exercise than the patients in the control group (Table II).

Discussion

About 500 MIBI SPECT stress tests are performed annually in our institution. Main indications are screening of patients with chest pain or positive stress tests to exclude cardiac ischemia, assessment of prognosis after successful percutaneous transluminal coronary angioplasty and coronary artery bypass graft, or perioperative risk evaluation prior to noncardiac surgery. The high sensitivity but relatively low specificity of MIBI SPECT has been described earlier.[1] However, few data are available regarding the impact of clin-

TABLE I Baseline clinical characteristics

	Study group (n = 41)	Control group (n = 41)	p Value
Age	59 ± 9	60 ± 9	0.83
Female (%)	16 (39)	16 (39)	
Body mass index	28 ± 4	28 ± 6	0.18
History of smoking (%)	11 (27)	16 (39)	0.24
Diabetes (%)	1 (2)	4 (10)	0.15
Hyperlipidemia (%)	13 (32)	27 (66)	0.002
Hypertension (%)	20 (49)	11 (27)	0.04
Left ventricular hypertrophy (%)	18 (44)	9 (22)	0.05
LBBB (%)	3 (7)	3 (7)	
LAFB (%)	7 (17)	0	0.005
ST-segment depression (%) [a]	7 (17)	15 (37)	0.05
Chest pain (%) [a]	6 (15)	12 (29)	0.02
DIP stress test (%)	11 (27)	14 (34)	0.47
Coronary artery anatomy			
Coronary 1-vessel disease (%) [b]		6 (15)	
Coronary 2-vessel disease (%) [b]		12 (29)	
Coronary 3-vessel disease (%) [b]		23 (56)	
Angiographically normal coronary arteries (%) [b]	26 (63)		

Data are numbers and percentages or mean values ± (standard deviation) where appropriate.
[a] = During exercise.
[b] = Coronary artery stenosis > 50.
Abbreviations: LBBB = left bundle branch block, LAFB = left anterior fascicular block, DIP = dipyridamole.

TABLE II Analysis of sestamibi uptake defects

	Study group (n = 41)	Control group (n = 41)	p Value
LAD MIBI uptake defect			
Fixed (%)	3 (7)	9 (22)	0.06
Reversible (%)	26 (63)	20 (49)	0.18
Cx MIBI uptake defect			
Fixed (%)	1 (2)	4 (10)	0.15
Reversible (%)	4 (10)	15 (37)	0.003
RCA MIBI uptake defect			
Fixed (%)	4 (10)	16 (39)	0.002
Reversible (%)	15 (37)	23 (56)	0.08
MIBI uptake defect (total)			
Fixed (%)	6 (15)	21 (51)	0.0003
Reversible (%)	41 (100)	41 (100)	
Mild MIBI uptake defects (%)	12 (29)	4 (10)	
Moderate MIBI uptake defects (%)	26 (63)	20 (49)	0.0004
Severe MIBI uptake defects (%)	3 (7)	17 (41)	

Data are numbers and percentages of patients.
Abbreviations: LAD = left anterior descending artery, Cx = circumflex artery, RCA = right coronary artery, MIBI = sestambi.

ical findings in patients with abnormal MIBI SPECT without significant coronary diameter stenoses. Artefacts due to suboptimal count density, soft tissue attenuation, and technical problems are well known reasons for so-called "false-positive" MIBI SPECT.[2]

One limitation of the present study was that coronary angiography was not performed routinely in patients with normal MIBI scans. Calculations of sensitivity and specificity rates could therefore not be performed.

The main findings of our study were that LV hypertrophy and LAFB were associated significantly more with abnormal MIBI scans without significant coronary artery diameter stenoses than with an age- and gender-matched control group with angiographically significant stenoses. False septal MIBI uptake defects in patients with LBBB have been described by several investigators.[7–10] It has been shown that LBBB itself may reduce myocardial perfusion and glucose uptake in the septum because of impaired systolic thickening and augment-

ed intramyocardial pressure in the septum without relation to septal ischemia.[11] In this setting, pharmacologic stress tests with adenosine or dipyridamole have been recommended for better interpretation of MIBI scans.[12–15] In this study, MIBI uptake defects in patients with LAFB were located in the basal septal segment in three cases, the inferobasal segment in three, and the anteroapical segment in one. Tracer uptake defects in myocardial regions other than septal regions can therefore hardly be explained by a conduction defect or reduced myocardial perfusion due to impaired systolic thickening of the septum alone.

Concerning LV hypertrophy, data on analysis of MIBI scans for prediction of significant CAD are contradicting. Due to the low specificity of scintigraphy in LV hypertrophy, some investigators recommend that stress echocardiography should be the method of choice for assessing myocardial perfusion in these patients.[12] Others found that hypertensive patients, with or without LV hypertrophy, should not be excluded from stress myocardial perfusion scintigraphy.[13] Some investigators believe that vasodilation with dipyridamole allows for semiquantitative assessment of reduced myocardial perfusion reserve, yielding positive MIBI scans in patients with microvascular disease without significant coronary diameter stenosis.[14, 15] In our study group, dipyridamole stress test has only been performed in 39% (7/18) of patients with LV hypertrophy showing MIBI uptake defects without CAD.

Recently, Verna *et al.*[16] demonstrated an abnormal vasodilation capacity of the coronary circulation and angiographically unrecognized coronary atherosclerosis assessed by intracoronary Doppler velocity measurements and intracoronary sonography in a relatively high percentage of patients with so called "false positive" MIBI SPECT. Only patients with chest pain, abnormal stress exercise test, and coronary artery stenoses < 50% were included. Coronary flow reserve measurements or intravascular ultrasound investigations were not performed in this study. Of the 41 patients with "false positive" MIBI uptake defects, 15 (37%) showed minor coronary artery stenoses (< 50%) at angiography, whereas the remaining 26 patients had angiographically normal coronary arteries. In all 15 patients with minor coronary artery stenoses (< 50%) LV hypertrophy was present; this suggests microvascular disease at least in these patients. On the other hand, only 3 of the 26 patients with angiographically completely normal coronary arteries showed LV hypertrophy on echocardiography. This suggests some mechanisms other than only microvascular disease for "false-positive" MIBI uptake defects in this group.

Conclusion

Of 270 patients referred to coronary angiography due to reversible MIBI uptake defects, 26 (9.6%) showed angiographically normal coronary arteries and 15 (5.6%) had no significant coronary artery diameter stenoses (< 50%). In these 41 patients, we found a significantly higher proportion of LV hypertrophy and LAFB than in an age- and gender-matched control group of patients with MIBI uptake defects due to significant CAD. This suggests that microvascular disease, the presence of angiographically underestimated CAD, and conduction abnormalities with reduced myocardial perfusion due to impaired systolic thickening of the septum may play an important role in so-called "false-positive" MIBI scans. Therefore, the term "false-positive" uptake defects may lead to the unjustified clinical assumption of a nonexisting heart disease and should not be used in clinical practice. In patients with MIBI uptake defects without angiographically detectable CAD microvascular disease, angiographically underestimated CAD, and conduction abnormalities should be considered for proper interpretation of MIBI scans.

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