

Prevalence and Angiographic Significance of Normal Myocardial Perfusion SPECT With Positive Exercise Electrocardiogram

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In a consecutive series of 7350 myocardial perfusion SPECT studies, 66 (0.9%) nonrevascularized patients with a normal resting ECG had normal scintigraphic findings with a positive ECG in the exercise test. We retrospectively analyzed 33 patients with coronary angiography, 26 of whom were women ($P < .000$). Twenty one of the 26 women (81%) and 1 of the 7 men (14%) had normal coronary angiographic findings ($P = .004$). Seven out of 11 patients with coronary heart disease had left main coronary artery or multivessel disease. We conclude that the "normal SPET with positive ECG" pattern is infrequent, and is observed predominantly in women with normal coronary angiographic findings. However, severe coronary artery disease cannot be ruled out in these patients, and this pattern should be considered a possible indication for coronary angiography.

Key words: *Scintigraphy. Exercise test. Coronary angiography. Coronary artery disease.*

Prevalencia y significado angiográfico de la SPECT de perfusión miocárdica normal con electrocardiograma de esfuerzo positivo

De una serie consecutiva de 7.350 estudios con tomografía computarizada por emisión de fotones simples (SPECT) de perfusión miocárdica, 66 pacientes (0,9%) con un electrocardiograma (ECG) de base normal y no revascularizados presentaron un estudio gammagráfico normal junto con un ECG positivo en la prueba de esfuerzo. En este estudio analizamos retrospectivamente a los 33 enfermos con estudio coronariográfico, de los cuales 26 eran mujeres ($p < 0,000$). En un 81% de las mujeres (21/26) frente a sólo un 14% de los varones (1/7), la coronariografía era normal ($p = 0,004$). De los 11 pacientes con enfermedad coronaria, 7 tenían estenosis de más de un vaso o del tronco común. Así pues, el patrón «SPECT negativa con ECG positivo» es infrecuente y se observa un predominio en mujeres con coronarias angiográficamente normales. No obstante, en estos enfermos no se puede excluir con seguridad una enfermedad coronaria severa y, por este motivo, debería considerarse la indicación de una coronariografía.

Palabras clave: *Gammagrafía. Prueba de esfuerzo. Coronariografía. Enfermedad coronaria.*

INTRODUCTION

A number of authors have demonstrated that patients with chest pain and negative myocardial perfusion scintigraphy results have a good prognosis with <1% per year mortality and incidence of infarction.¹⁻¹⁰ However, exceptions do appear in the literature and

others report a history of ischemic heart disease,^{11,12} diabetes in women,¹² low exercise heart rate,¹¹ cardiomegaly,¹³ and sometimes a correlation with positive exercise electrocardiogram (ECG).¹⁴

To determine the prevalence of negative myocardial perfusion single-photon emission computerized tomography (SPECT) results associated with positive exercise ECG and its significance in terms of coronary angiography, we reviewed all SPECT studies performed in our center over a period of 8 years.

PATIENTS AND METHODS

We conducted a retrospective evaluation of 7350 myocardial perfusion SPECT studies performed in our

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center between 1994 and 2002. In total, 294 (4%) patients had normal SPECT and positive exercise ECG (horizontal or descending ST-segment depression ≥ 1 mm at 0.08 s after the J-point) (Table 1). We excluded patients with possible false-positive ECG (76 with abnormal baseline repolarization, 34 with intraventricular conduction disturbances, 18 with pacemakers, and 41 taking digitalis) and revascularized patients ($n=59$), leaving 66 with normal baseline ECG, normal SPECT and positive exercise ECG. For the present study, we selected 33 patients referred for coronary angiography by the clinical cardiologist.

Myocardial Perfusion SPECT With Combined Techniques

All patients underwent symptom-limited bicycle exercise test. A short protocol was followed (exercise-rest on one day only) with ^{99m}Tc -tetrofosmin. Tomographic images of short, horizontal, and long vertical axis projections were obtained with an Eslcint SP4 gamma camera with high resolution collimator. All SPECT studies were considered normal after qualitative evaluation in a nuclear cardiology session involving 2 experts from each specialty. All images were subsequently reviewed for possible presence of multiple vessel disease indicated by pulmonary uptake and/or left ventricular ischemic dilatation.

Cardiac Catheterization

All patients underwent coronary angiography using Seldinger's technique at ≤ 6 months after SPECT, assuming no previous complications. At least 2 projections were obtained to evaluate left and right main coronary arteries.

RESULTS

Results of SPECT assessment and exercise ECG for all 7350 patients are in Table 1. We enrolled 33 patients after excluding those with possible false-positive ECG, revascularization, without coronary angiography or with coronary angiography at >6 months after SPECT, and with no complications during this period. Of these 33 patients, 26 were women ($P<.000$); 23 (70%) had at least one risk factor (15, hypertension; 11, dyslipidemia, 6, type 2 diabetes, and 4, smoking).

TABLE 1. Results of Exercise ECG and Myocardial Perfusion SPECT in 7350 Studies*

ECG	Negative	Negative	Positive	Positive
SPECT	Negative	Positive	Negative	Positive
	2058 (28%)	3234 (44%)	294 (4%)	1764 (24%)

*ECG indicates electrocardiogram; SPECT, single-photon emission computerized tomography.

Prevalence of risk factors was somewhat lower (59%) among the 33 patients without coronary angiography but this was not statistically significant.

Exercise test and coronary angiography findings for these patients appear in Tables 2 and 3. Pulmonary uptake or transient ischemic dilation of the left ventricle were not found in any patient. At exercise testing, 10 women and 1 man were not taking anti-angina medication; 11 patients (7 women) were taking beta-blockers; 11 patients (10 women), calcium antagonists; 11 patients (10 women), nitrates, and 16 patients (10 women), antiplatelet drugs. Ten of the 26 women (38.5%) and 2 of the 7 men (28.6%) presented angina during exercise testing.

Ejection fraction was normal in all patients. A total of 21 of the 26 women (81%) had normal coronary angiography, compared with 1 of the 7 men (14%) ($P=.004$). One of the 5 women with coronary heart disease had 40% stenosis of the left main coronary artery and 1 had 2-vessel disease. One of the 6 men with coronary heart disease had 50% stenosis of the left main coronary artery and 4 had multivessel disease. None of the patients presented collateral circulation.

DISCUSSION

Prevalence of normal myocardial perfusion SPECT and positive exercise ECG is low: in our experience around 4%, similar to the 2%-3.5% range described elsewhere^{10,15,16}. When patients with possible false-positive ECG and revascularization are excluded, prevalence is $<1\%$,^{14,16} coinciding with our findings (0.9%).

As indicated previously^{14,15}, we have demonstrated that the pattern of "normal SPECT with positive exercise ECG" is principally found in women (26/33, 79.6%), in most of whom it is associated with angiographically normal coronary arteries (81% vs 14% of men; $P=.004$). These results are similar to findings reported by He et al¹⁶ in the only publication specifically to evaluate coronary angiography results in 52 patients with normal 201Tl SPECT scans and very positive exercise ECG (horizontal or downsloping ST-segment depression ≥ 2 mm). He et al found 80% of men had significant coronary stenosis by comparison with only 24% of women ($P<.0001$).

One possible cause of false-negative myocardial perfusion SPECT studies may be the presence of diffuse coronary heart disease with homogeneous ischemia of the entire left ventricle, perfusion images of which fail to identify any single region with comparatively more reduced uptake. We found most patients (7/11) with coronary heart disease had multivessel disease or disease of the left main coronary artery, whereas the remaining 4 presented non-critical one-vessel disease. These results also coincide with He et al¹⁶

TABLE 2. Results of Exercise Test and Coronary Angiography in the Group of 26 Women*

MET (1)	HR, %	SBP, mm Hg	Angina	ST, mm	MET (2)	Leads With Downsloping ST	ST Duration, min	Coronary Angiography
5	91	180	No	2	4.3	V ₄₋₆	10	Normal
4	73	150	Yes	1	4	Inf, V ₂₋₅	3	Normal
4.5	66	190	Yes	1	4.5	Inf	3	Normal
5.4	83	185	Yes	2	5.4	Inf, V ₄₋₆	5	Normal
5.4	81	180	No	1	4.3	Inf, V ₄₋₆	3	Normal
5.6	100	140	No	1	4.3	V ₄₋₅	1	Normal
4	72	150	Yes	1	4	V ₃	3	50% CX
3.5	82	190	No	1	3.5	Inf, V ₄₋₆	5	Normal
7	92	130	Yes	2	5	Inf, V ₄₋₆	3	Normal
4	60	200	Yes	1	4	D ₁ , Inf, V ₄₋₆	3	40% LMCA
10	82	160	No	1	7	V ₄₋₅	1	Normal
7	90	170	Yes	1	5	V ₄₋₆	7	Normal
7	105	170	No	1.5	5	Inf, V ₅₋₆	3	Normal
6	90	200	No	1	6	Inf, V ₅₋₆	1	Normal
6	85	210	No	1.5	6	Inf, V ₄₋₆	3	Normal
6.5	86	190	Yes	1	6.5	Inf, V ₅₋₆	1	Normal
5.6	81	220	Yes	1	5.6	D ₁ , V ₅	3	70% LAD, 60% IB
8	78	190	Yes	1.5	6.3	V ₅₋₆	3	60% LAD
7.3	83	200	No	1	7.3	Inf, V ₄₋₆	1	Normal
6	81	200	No	1	6	V ₄₋₆	1	70% LAD
6	80	160	No	1.5	6	Inf, V ₅	1	Normal
6	82	180	No	1	6	Inf, V ₅₋₆	1	Normal
7.3	97	170	No	1	5	Inf, V ₅₋₆	3	Normal
4.6	106	130	No	2.5	4.6	D ₁ , aVL, Inf, V ₄₋₆	3	Normal
5.7	87	160	No	2	5.7	V ₅₋₆	1	Normal
7	106	170	No	1.5	7	V ₅	1	Normal

*CX indicates circumflex; LAD, left anterior descending artery; ST duration, duration of downsloping ST-segment after exercise; HR, percentage of heart rate above theoretical maximum; Inf, leads on inferior surface; MET (1), maximum O₂ consumption; MET (2), O₂ consumption at onset of downsloping ST-segment; SBP, maximum systolic blood pressure; IB, intermediate branch; ST, maximum ST-segment downslope; LMCA, left main coronary artery.

who report 50% of patients with coronary heart disease presented significant stenosis of more than 1 vessel.

The low prevalence of patients with normal SPECT and positive ECG, greater presence of women, and high percentage of normal coronary angiographic fin-

TABLE 3. Results of Exercise Test and Coronary Angiography in the Group of 7 Men*

MET (1)	HR, %	SBP, mm Hg	Angina	ST, mm	MET (2)	Leads With Downsloping ST	ST Duration, min	Coronary Angiography
10	86	210	Yes	1	5	Inf, V ₄₋₅	3	80% Diag, 85% RCA, 90% PD
7	80	165	No	3	5	Inf, V ₄₋₆	7	70% LAD, 85% CX, 40% RCA, 50% IB
7.5	81	215	No	2	6.3	V ₄₋₆	1	Normal
8.8	74	200	No	2	7.7	Inf, V ₅₋₆	3	50% LAD, 90% CX, 80% Diag
7.3	53	200	No	2.5	5	Inf, V ₄₋₆	3	50% LAD, 90% Diag, 50% CX, 60% RCA
7	80	190	No	1.5	6.3	Inf, V ₅₋₆	1	75% CX, 85% OM
6	89	220	Yes	1.5	5	Inf, V ₅	3	50% LMCA

*RCA indicates right coronary artery; CX, circumflex; LAD, left anterior descending artery; Diag, diagonal; PD, posterior descending; ST duration, duration of downsloping ST-segment after exercise; HR, percentage of heart rate above theoretical maximum; Inf, leads on inferior surface; MET (1), maximum O₂ consumption; MET (2), O₂ consumption at onset of downsloping ST-segment; OM, obtuse marginal; SBP, maximum systolic blood pressure; IB, intermediate branch; ST, maximum downsloping ST-segment; LMCA, left main coronary artery.

dings in women, explain the generally good prognosis for patients with negative myocardial perfusion SPECT, independently of exercise ECG results. However, it is clear that severe coronary heart disease may be present when normal SPECT is associated with positive exercise ECG, suggesting this should be considered an indication for coronary angiography.

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