Original article

Detection of left ventricular hypertrophy by Tc-99 tetrofosmin gated-SPECT

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RESUMEN

Introducción: La hipertrofia concéntrica del ventrículo izquierdo (HVI) es un riesgo cardiovascular independiente para eventos como muerte súbita cardiaca, infarto del miocardio y enfermedad cerebrovascular. El objetivo de este estudio fue determinar la especificidad, sensibilidad, valor predictivo positivo (VPP) valor predictivo negativo (VPN) y exactitud de Tc-99 – SPECT sincronizado al ECG, para la detección de HVI.
Métodos: Pacientes enviados por presencia o sospecha de enfermedad coronaria que fueron sometidos a estudio con Tc-99–SPECT y que contaran con un ecocardiograma (ECO) realizado dentro de los dos meses previos al estudio fueron prospectivamente incluidos en el estudio. El grupo consistió de 52 pacientes, 25 hombres, con una edad media de 64.5 ± 12 años.
Resultados: Cuando la HVI fue definida por ECO como un grosor medio de la pared septal anterior en diástole + pared posterior del VI en diástole /2 > 11 MM, el SPECT tuvo una sensibilidad y especificidad de 91% y 33% respectivamente, con un VPP de 94%& y VPN de 48% y exactitud de 58%. Cuando la HVI fue definida como una relación grosor/radio del ventrículo izquierdo (h/r) > 0.45, el método mostró una especificidad de 95%, sensibilidad de 37% y VPP de 97% y VPN de 54% con exactitud de 62%. En hombres, cuando los criterios para HVI fueron una masa de> 11 g/m^2, la especificidad y sensibilidad para el método fueron de 100% y 20% con VPP, VPN y exactitud de 100%, 45% y 48%, respectivamente. En mujeres, cuando la HVI fue definida como una masa > 106 g/m^2, el SPECT tuvo una especificidad de 91% y sensibilidad de 44%, VPP de 94% y VPN y exactitud de 42% y 63%. Si el criterio para HVI fue de masa >125 g/m^2, el SPECT tuvo especificidad y sensibilidad de 86% y 30% respectivamente, y un VPP de 85%, VPN de 64% con exactitud de 62%.

Palabras clave: ventrículo izquierdo, hipertrofia, Tc-99 tetrofosmin.

ABSTRACT

Introduction. Left ventricular hypertrophy (LVH) is a strong cardiovascular risk factor and an independent major cardiac risk factor for sudden cardiac death, myocardial infarction and stroke. The objective of this study was to determine the specificity, sensitivity, positive predictive value (PPV) Negative Predictive Value (NPV) and accuracy of a Tc-99 gated-SPECT method for detecting LVH.
Methods: Patients referred for evaluation of known or suspected CAD, who underwent myocardial perfusion SPECT imaging with Tc-99 Tetrofosmin and who had also an echocardiogram performed within the previous 2 months were prospectively enrolled in the study. The group consisted of 52 patients, 25 men and 27 women, the mean age was 64.5 ± 12 yrs.
Results: When the echocardiographic LVH was defined as a mean wall thickness VSTd + PWTd/2 ≥ 11mm, the SPECT method had a specificity and sensitivity of 91% and 33% respectively, a PPV of 94%, a NPV of 48% and an accuracy of 58%. When the LVH was defined as a thickness to radius ratio (h/r) >0.45, the SPECT Method showed a specificity of 95%, sensitivity of 37% and a PPV of 97% and NPV of 54% with an accuracy of 62% . In Men, when the LVH criteria was a LV Mass >111 g/m2, the specificity and sensitivity for the SPECT method criteria was 100% and 20% respectively with a PPV, NPV and Accuracy of 100%, 45% and 48%. In Women, when LVH was defined as a LV Mass >106 g/m2, the SPECT method had a specificity of 91% and sensitivity of 44%, a PPV of 94%, and NPV and Accuracy of 42% and 63%. If the criteria was a LV Mass >125 g/m2, SPECT showed a specificity and sensitivity of 86% and 30% respectively and a PPV of 85% and a NPV of 64% with an Accuracy of 62 %.

Key words: Left Ventricle, Hypertrophy, Tc-99 Tetrofosmin.

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Left ventricular hypertrophy (LVH) is the result of the left ventricle's adaptation to chronic pressure overload, volume overload, endocrine processes[1] or a specific myocardial disease. In the general population, hypertension is the most common cause of LVH, which was recognized as a strong cardiovascular risk factor early in the Framingham study.[2] In that study, LVH was determined by electrocardiographic (ECG) criteria, and was found to be associated with increased overall mortality rates. LVH is also an independent major cardiac risk factor for sudden cardiac death, myocardial infarction and stroke.[3-4] The presence of coronary heart disease (CHD) or congestive heart failure might be aggravated by LVH.[1]

Several ECG criteria in addition to the Framingham criteria are in clinical use, and the ECG has been suggested as a valuable tool for detecting LVH at a lower cost when compared to echocardiography, which is a direct assessment of LV wall thickness and cavity dimensions, but it is only recommended for a subset of patients as an initial screening tool.[5,6]

Left ventricular hypertrophy is not always pathological; it is common in healthy athletes. Additional data might be necessary to distinguish between a pathological and a non pathological LVH.[7] Echocardiography is the most common way to obtain such information.[2,8]

It is common in myocardial perfusion studies to observe patients where the myocardial walls appear thick and the left ventricular cavity small, raising the question whether such patients could have LVH, an important additional observation given the above prognostic implications. The objective of this study was to determine the ability of a new Tc-99 gated-SPECT method to detect LVH, and compare the method's diagnostic performance with the clinically used ECG criteria for LVH, using common echocardiographic criteria as the reference.

PATIENTS AND METHODS

Patient population

Pilot group

Patients referred for evaluation of known or suspected CAD, who underwent myocardial perfusion SPECT imaging with Tc-99 Tetrofosmin, and who had also an echocardiogram performed within 2 months were prospectively enrolled in the study. Patients were excluded if gated-SPECT could not be performed, if disproportionate septal hypertrophy existed, if the patient had large perfusion defects in the rest scan (i.e. more than 40 percent decreased tracer uptake in a myocardial wall when compared with the best perfused wall). The group consisted of 52 patients, 25 men and 27 women, the mean age was 64.6 ±12 yr. (Table 1)

Echocardiographic measurements

All the patients underwent echocardiographic study within 2 months of their perfusion imaging study. Two-dimensionally guided LV M-mode recordings were obtained using a commercially available echocardiograph with a 2.5 MHz transducer, according to the recommendations of Devereux et al.[9] For each measurement and tracing, a minimum of three cardiac cycles was used. M-mode left ventricular chamber dimensions were measured from parasternal long-axis views according to specifications of the American Society of Echocardiography.[10] The measurements included LV internal diameter at end-diastole (LVIDd), end-systole, the ventricular septal thickness at end-diastole (VSTd), and the posterior wall thickness at end-diastole (PWTd). Diastolic measurements were used to calculate the VSTd/PWTd ratio, and LV mass, according to Devereux:[11]

Table 1. Demographic data of the patients

	Male	*Female*	*Total*	*p*
Sex (n)	25	27	52	NS
Age (years)	64 ± 12	55 ± 9	64.6 ± 12	NS
BSA (g/m²)	1.99 ± 0.3	1.81 ± 0.1	1.90 ± 0.3	< 0.01
Systolic BP (mm/Hg)	136 ± 13	143 ± 25	139 ± 20	NS
Diastolic BP	82 ± 9	81 ± 11	82 ± 10	NS
Echo EDD (mm)	54 ± 9	46 ± 6	50 ± 8	0.01
Echo ESD (mm)	40 ± 10	30 ± 5	35 ± 9	0.001
Echo EF%	52 ± 11	57 ± 12	54 ± 12	NS
Nuclear EF%	49 ± 12	59 ± 16	54 ± 15	0.02
ESV (mL)	67 ± 32	35 ± 26	50.7 ± 33	0.001
EDV	128 ± 42	77 ± 30	101.3 ± 44	< 0.001
SV	61 ± 19	41 ± 11	51 ± 18	< 0.001
LV Mass (g/m²)	131 ± 49	117 ± 48	123 ± 49	NS
Echo thickness (mm)	11.6 ± 1.9	11.7 ± 3	11.7 ± 2.2	NS

0.80 x {1.04 x [(septal thickness + LV internal diameter + posterior wall thickness)^{3} - (LV internal diameter)^{3}]} + 0.6 g and normalized by body surface area.

Definition of LVH

a) a mean left ventricle wall thickness (IVSTd+PWTd /2) of > 11 mm;
b) a thickness to LV cavity radius ratio ≥ 0.45 (half of the LVIDd divided by the LV mean diastolic wall thickness in mm),[12] (reference)
c) LV Mass indexed by body weight >106 g/m^2 in women and >111 g/m^2 in men
d) Overall LV mass indexed by body weight >125 g/m^2.

Myocardial perfusion imaging

A stress-rest imaging protocol was used. Eight mCi Tc-99m Tetrofosmin was administered at peak stress (defined as maximal possible effort, moderately severe chest pain, dyspnea or fatigue) and the test continued for 30-60 seconds. Stress imaging was performed 20-40 min post tracer administration. Two to 3 hours later 24 mCi Tc-99m Tetrofosmin was injected rest. Rest imaging was performed 20-40 min post tracer administration.

A 3-headed gamma-camera (Prism, Picker Int., Cleveland Ohio) equipped with high resolution collimators was used. Data were acquired in 64x 64 matrix, over 180° from LPO 45 to RAO 45, 32 angles, 25 sec/angle for the stress study, and 20 sec/angle for the rest study. All studies were reconstructed using filtered back projection (ramp). A low pass filter was applied (order 0.5 with cutoff 0.33 for rest studies and order 0.5 with cutoff 0.25 for stress studies). The data were reformatted to vertical long, short and horizontal long axis (6 mm) according to the individually determined anatomical cardiac long axis. Software zoom was applied for display and visual assessment purposes, and coronal slices were added hereby generating perfusion images representing regional myocardial perfusion in the basal, mid and apical thirds of the myocardium. Midventricular sagittal and transaxial slices were also created for visualization of the apex and the walls in longitudinally context. The stress and rest studies were carefully aligned to insure that the myocardial segments in both studies was compared. The two studies were displayed simultaneously on a high resolution monitor using a standard color table for visual semiquantitative analysis.

The rest SPECT acquisition was acquired on a gated study divided into 8 frames with an acceptance window of ± 10% around the mean R-R interval during 1 minute prior to the study.

Left ventricular size evaluation

A short axis mid-ventricular slice, approximate at the level of insertion of the papillary muscles was selected and a pixel area from the external and internal borders was obtained (Figure 1). Two methods were used: The ratio of the external area divided by the internal cavity area was defined as SPECT method.

Using a ROC curve analysis we obtained a SPECT threshold for abnormality of an external to internal pixel area ratio ≥ 16.

ECG measurements

A 12-lead ECG was recorded prior to the stress test in all subjects at a 25mm/second and 1mV/cm calibration. The patient was considered as having LVH by ECG when any of the following criteria were met:

a) Sokolow-Lyon[13] (sum of the amplitudes of the S wave in lead V_1 and the R wave in V_5 and V_6 >35 mm).
b) Gender-specific Cornell voltage criteria[14] (SV_3 + R aVL > 28 mm in men and >20 mm in women).
c) Framingham Criteria[15] (coexistence of a definite strain pattern and at least one of the following: sum of the amplitudes of the S wave in lead III and the R wave on lead I >25 mm, sum of the S wave

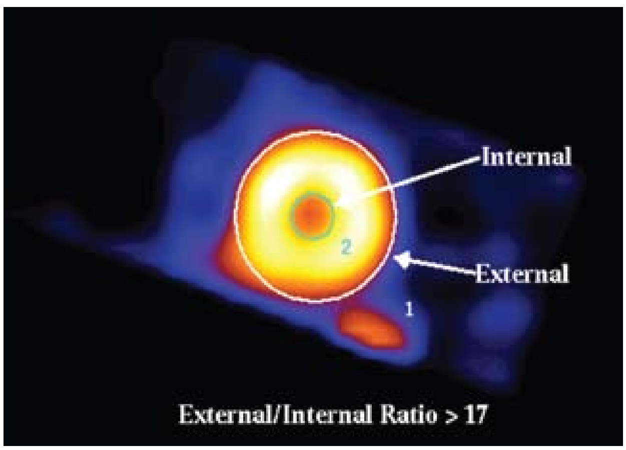

Figure 1.

amplitude in V_1 or V_2 and the amplitude of the R wave in V5 or V_6 >35 mm, S wave in V1 or R in V_6 >25mm.

RESULTS

Prevalence of LVH

The prevalence of LVH in the pilot group according to the 4 different echocardiographic LVH criteria ranged from 44% to 60% (Table 2).

Electrocardiographic Framingham criteria evidence of LVH was found overall in 7% to 24% of the population studied (Table 3). LVH by Sokolow criteria was found in 4% to 20% of the patients, and LVH by Cornell criteria was found in 7% to 20%.

The SPECT-1 method showed a prevalence of LVH of 12% to 21% of the cases.

SPECT method performance

When the echocardiographic LVH was defined as a mean wall thickness VSTd + PWTd/2 ≥ 11mm, the SPECT method (≥16) showed a specificity and sensitivity of 91% and 33% respectively, a PPV of 94%, a NPV of 48% and an accuracy of 58% (Table 4). When the LVH criteria used was a thickness to radius ratio >0.45, the SPECT method showed a specificity and sensitivity of 95% and 37% respectively and a PPV of 97%, a NPV of 54% and an accuracy of 62% (Table 3).

If the echocardiographic diagnosis of LVH was defined as follows: In men, the LVH echocardiographic criteria of LV mass >111 g/m^2 allowed a specificity and sensitivity for the SPECT method criteria 100% and 20% respectively with a PPV, NPV and accuracy of 100%, 45% and 48% respectively (Table 5).

In women, when LVH was defined as a LV mass >106 g/m^2, the SPECT method had a specificity of 91% and the

Table 2. Prevalence of LVH according to he different echocardiographic thresholds

	Echo T/R > 0.45	*Echo > 11*	*LV mass > 106g/m^2(F)*	*LV mass > 111g/m^2(M)*	*LV mass > 125g/m^2*
Framingham	13.46%	13.46%	7.41%	24%	9.62%
Sokolow	9.62%	9.62%	3.70%	20%	8%
Cornell	11.5%	13.46%	7.41%	20%	11.54%
SPECT 1 (≥16)	21.15%	19.23%	25.93%	12%	13.46%

SPECT 1: External area in pixels divided by internal area in pixels.

Table 3. Diagnostic performance of common ECG criteria and SPECT in 52 patients

	Sensitivity (SENS)	*Specificity (SPEC)*	*Positive predictive value*	*Negative predictive value*	*Accuracy*
Framingham	23%	91%	94%	49%	52%
Sokolow	17%	91%	94%	47%	48%
Cornell	20%	91%	94%	48%	50%
SPECT 1 (≥ 16)	37%	95%	97%	54%	62%

SPECT 1: External area in pixels divided by internal area in pixels.

Table 4. Comparison of diagnostic performance of common ECG criteria for LVH, criteria in 52 patients

	Sensitivity (SENS)	*Specificity (SPEC)*	*Positive predictive value*	*Negative predictive value*	*Accuracy*
Framingham	23%	91%	94%	49%	52%
Sokolow	17%	91%	94%	47%	48%
Cornell	23%	95%	97%	49%	54%
SPECT 1 (≥ 16)	33%	91%	94%	48%	58%

SPECT 1: External area in pixels divided by internal area in pixels.

highest sensitivity (44%), when compared to the different ECG criteria. There was no difference in the PPV of 94%, but there was a higher NPV and accuracy (42% and 63%) with that of the ECG criteria (Table 6). When the criteria for LVH was a LV mass >125 g/m^2, the SPECT 1 method (≥16) showed a specificity and sensitivity of 86% and 30% respectively and a PPV of 85% and a NPV of 64% with an accuracy of 62% (Table 7).

Electrocardiographic performance

When LVH was defined as a mean wall thickness VSTd/PWTd ≥ 11mm, we found a specificity and sensitivity of 91% and 23% respectively for the Framingham criteria, with a PPV of 94% and a NPV of 47% and an accuracy of 52%. The Sokolow criteria had a specificity and sensitivity of 91% and 17%, with both PPV and NPV of 91% and 47% and an accuracy of 48%. The Cornell criteria showed a specificity and sensitivity of 95% and 23%, with a PPV, NPV and accuracy of 94%, 48% and 54% respectively (Table 4).

In men, when the criteria for LVH was a left ventricular mass >111g/m^2, the specificity and sensitivity for the ECG LVH criteria was 100% and 40% respectively for the Framingham criteria, a PPV and NPV of 100% and 53% respectively and an accuracy of 64%. The Sokolow criteria had a specificity and sensitivity of 100% and 33% with a PPV of 100% and a NPV of 40% and accuracy of 60%. The Cornell criteria showed a specificity of 100% and a sensitivity of 33%, with a PPV, NPV and accuracy of 100%, 50% and 60% respectively (table 5).

LVH defined as a left ventricular mass >106 g/m^2 in Women, Framingham criteria showed a specificity and sensitivity of 91% and 12% respectively, a PPV and NPV of 94% and 44% and an accuracy of 44%. Sokolow criteria showed a specificity and sensitivity of 91% and 6% and a PPV of 94%, NPV of 42% and an accuracy of 41%. The Cornell criteria showed a specificity of 91% and a sensitivity of 12%, with PPV and NPV of 92% and 63% respectively and an accuracy of 44% (Table 6).

When the threshold for LVH was defined as: LV mass >125 g/m^2, the specificity and sensitivity for the ECG LVH criteria was 86% and 22% respectively for the Framingham criteria, a PPV and NPV of 85% and 62% respectively. The Sokolow criteria had a specificity and sensitivity of 90% and 17% with a PPV of 88% and a NPV of 60%. The Cornell criteria showed a specificity of 93% and a sensitivity of 26%, with a PPV, a NPV of 92% and 63% respectively an accuracy of 62% (Table 7).

If LVH was defined as a thickness to radius ratio ≥ 0.45, the specificity and sensitivity for the ECG LVH criteria in our population was 91% and 23% respectively for the Framingham criteria, a PPV, NPV and accuracy of 94%, 49% and 52% respectively. The Sokolow showed specificity and sensitivity of 91% and 17% with a PPV of 94% and

Table 5. Diagnostic performance of common ECG criteria and SPECT (n = 52)

	Sensitivity	*Specificity*	*Positive predictive value*	*Negative predictive value*	*Accuracy*
Framingham	40%	100%	100%	53%	64%
Sokolow	33%	100%	100%	44%	60%
Cornell	33%	100%	100%	50%	60%
SPECT 1 (≥ 16)	20%	100%	100%	45%	48%

SPECT 1: External area in pixels divided by internal area in pixels.

Table 6. Diagnostic performance of common ECG criteria and SPECT (n = 52)

	Sensitivity (SENS)	*Specificity (SPEC)*	*Positive predictive value*	*Negative predictive value*	*Accuracy*
Framingham	12%	91%	94%	44%	44%
Sokolow	6%	91%	94%	42%	41%
Cornell	12%	91%	94%	44%	44%
SPECT (≥ 16)	44%	91%	94%	55%	63%

SPECT 1: External area in pixels divided by internal area in pixels.

Table 7. Diagnostic performance of common ECG criteria and SPECT (n = 52)

	Sensitivity	*Specificity*	*Positive predictive value*	*Negative redictive value*	*Accuracy*
Framingham	22%	86%	85%	62%	58%
Sokolow	17%	90%	88%	60%	58%
Cornell	26%	93%	92%	63%	63%
SPECT 1 (≥ 16)	30%	86%	85%	64%	62%

SPECT 1: External area in pixels divided by internal area in pixels.

a NPV of 47% .The accuracy for this ECG method was 48%. The Cornell criteria had a specificity of 91% and a sensitivity of 20%, with a PPV and NPV of 94% and 48% respectively and accuracy of 50% (table 3).

Validation phase

Fifty patients were studied several weeks after the initial patient population was evaluated. The group consisted of 25 women and 25 men with an echocardiogram performed within < 2 months of the cardiac SPECT study. The patients did not have any perfusion abnormality at rest and were randomly chosen. A short axis slice at the approximate level of insertion of the papillary muscles was selected and a pixel area from the external and internal borders was obtained (Figure 1). The ratio of the external pixels divided by the internal cavity pixels (SPECT method) was used and a value ≥ 16 was defined as abnormal.

Twenty-one patients had echocardiographic signs of LVH (echo thickness ≥11 mm). The specificity of the SPECT method (ratio ≥ 16) was 82%, sensitivity 46%, predictive positive value 76% and negative predictive value of 56%.

DISCUSSION

Left ventricular hypertrophy is a strong independent predictor of adverse cardiovascular events, therefore, identification of those patients with LVH is critical to determine their therapeutic approach, since the regression of hypertrophy ensues a decrease in the risk of future events.[16] One of the most common methods to detect this subgroup of patients is electrocardiography, and several studies support its prognostic value, very low sensitivity, with a good specificity. Several factors interfere with the value of ECG to detect LVH and include the different criteria employed, sex, smoking, and obesity among others.[17]

Previous studies have shown a good correlation with LV size and volume determination with Tl-201,[18] to our knowledge, this is the first attempt to determine the presence of LVH with this method. Hypertension is commonly associated with coronary artery disease and LVH, and myocardial perfusion imaging with Tc-99 provides valuable information, which includes perfusion and left ventricular function. The value of adding such information, such as LVH is yet to be studied.

In our study, SPECT detection of left ventricular hypertrophy showed a similar specificity and a better sensitivity when compared to ECG criteria. The definition for LVH varies according to different authors, therefore, the results obtained in this analysis varies according to the echocardiographic definition of LVH. Other variables that suggest LVH include the visual appearance of thick ventricular walls and small cavity, the presence of a high tracer uptake by the papillary muscles and left ventricular apical thinning were very inconsistent in our population. One of the advantages of our method is that it can detect LVH even in the presence of cavity dilatation, as shown in table 3.

LIMITATIONS OF THE STUDY

This method has proven to be less sensitive and specific in the detection of left ventricular hypertrophy by direct measurements and by determination of pixel areas when compared to echocardiography which has been widely validated as a method accurate in detecting LVH. SPECT images provide an inaccurate definition of the endocardial and epicardial borders due to partial volume effect and scattering, especially in small hearts and in women. Processing tools such as filters that help decrease such technical limitations will help clear out the value of this methods to identify patients with left ventricular hypertrophy.

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