Clin. Cardiol. 26, 143–146 (2003)

Technetium-99m Sestamibi Cavity/Myocardium Count Ratio in the Detection of Left Ventricular Hypertrophy

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Summary

Background and hypothesis: Left ventricular hypertrophy (LVH) is an independent risk factor for cardiovascular mortality and morbidity. This study was designed to assess whether technetium-99m (^{99m}Tc) sestamibi cavity-to-myocardium count (c/m) ratio would differentiate LVH from normal geometry, and discriminate between the two patterns—concentric and eccentric—of LVH.

Methods: In all, 72 patients including 32 hypertensive patients with both normal ^{99m}Tc sestamibi single-photon emission computed tomography imaging and good-quality echocardiographic recordings were studied retrospectively. Four different patterns of left ventricular (LV) geometry were defined: normal (n = 47), concentric remodeling (n = 3), eccentric LVH (n = 13), and concentric LVH (n = 9).

Results: Left ventricular hypertrophy was detected in 22 of 32 hypertensive patients. The c/m ratio calculated on midventricular short-axis slices of dipyridamole-stress ^{99m}Tc sestamibi images was significantly decreased in patients with LVH compared with subjects with normal geometry (0.05 ± 0.02 vs. 0.17 ± 0.08, $p = 0.001$). A c/m ratio of < 0.124 yielded a sensitivity of 86%, a specificity of 64%, and an overall diagnostic accuracy of 68% for detecting LVH. Negative correlations of c/m ratio were found to LV mass-index ($r = -0.44$, $p = 0.004$), septal width ($r = -0.42$, $p = 0.008$), posterior wall thickness ($r = -0.39$, $p = 0.001$), and relative wall thickness ($r = -0.40$, $p = 0.001$). Multiple linear regression analysis revealed that LV mass index was the single independent predictor of c/m ratio. Although both groups with concentric and eccentric LVH had a significantly lower mean c/m ratio than those with normal geometry ($p = 0.01$ and $p = 0.01$, respectively), no significant difference of c/m ratio was found between the two patterns of LVH.

Conclusion: A new index, c/m ratio on ^{99m}Tc sestamibi images, has a potential to discriminate between LVH and normal geometry in subjects free of myocardial ischemia.

Key words: ^{99m}Tc sestamibi, cavity/myocardium count ratio, left ventricular hypertrophy

Introduction

Left ventricular hypertrophy (LVH) is an independent risk factor for cardiovascular disease morbidity and mortality in adults.[1–4] Its presence and patterns—concentric and eccentric—provide clinically useful information. The present study was performed retrospectively on dipyridamole stress (DS) technetium 99m (^{99m}Tc) sestamibi single-photon emission computed tomography (SPECT) images of subjects, including hypertensive patients who were all free of myocardial ischemia. Our purpose was to investigate whether ^{99m}Tc sestamibi cavity-to-myocardium count (c/m) ratio would differentiate echocardiographically determined LVH from normal geometry and discriminate between the two patterns—concentric and eccentric—of LVH.

Materials and Methods

Of patients referred to our department for clinically suspected coronary artery disease, 72 (35 men, 37 women; mean

This work was presented in part at 5th International Conference of Nuclear Cardiology, Vienna, Austria, May 2001.

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Received: November 1, 2001
Accepted with revision: March 20, 2002

age 47 ± 13 years, range 31–72) with both normal dipyridamole stress ^{99m}Tc sestamibi imaging and good quality echocardiographic recordings were selected. Scintigraphic and echocardiographic studies were performed within a 1-month period. No patient had any heart disease other than LVH detected by echocardiography; 32 had a history of hypertension and were on antihypertensive therapy administered by the outpatient clinic of our institute. The remaining 40 individuals were free of hypertension and had normal systolic and diastolic blood pressures as measured by cuff sphygmomanometer at scintigraphic examination.

All patients underwent standard 1-day DS-rest ^{99m}Tc sestamibi SPECT myocardial perfusion scintigraphy.[5] Dipyridamole stress testing was performed with 0.56 mg/kg dipyridamole intravenously over a 4-min period. Four min later, 10 mCi of ^{99m}Tc sestamibi was injected and SPECT images were collected after 45 min. A gamma camera (Philips, Eindhoven, the Netherlands) equipment with high-resolution collimator and a 20% window centered at the 140 keV photopeak of ^{99m}Tc was used. Using 64 × 64 matrices, 32 projections, 30 s each, were acquired in step-and-shoot mode over a 180˚ arc. The image reconstruction was performed with ramp and Metz filter. No attenuation or scatter correction was used. The transaxial slices were realigned along the heart axis obtaining short-axis, horizontal, and vertical long-axis slices. The DS stress images were examined for the presence of perfusion defects and were classified as normal if no perfusion defect was seen in any segments. The short-axis tomogram from the mid ventricle was used for computation of the c/m ratio. A 5 × 5 pixel (1 pixel = 6.25 mm) rectangular region of interest was placed in the visually determined center of the left ventricular (LV) cavity (c) and the mean count per pixel was obtained. The region of interest (ROI) was moved to the hottest area of the LV wall (m) using overrange blank for identification. The ratio of counts in the LV cavity to that in the myocardium was calculated as the c/m ratio.

Echocardiographic examinations were performed on each subject by using a commercially available system equipped with a 2.5 MHz transducer. Left ventricular diameters and volumes, wall thicknesses, fractional shortening, and ejection fraction were measured by previously described methods. Left ventricular mass was calculated using the following formula with all indices measured at end-diastole: LV mass = 0.8 [1.04 (LV diameter + septal thickness + posterior wall thickness) ^{3} − (LV diameter) ^{3}] + 0.6.[6] Relative wall thickness (RWT) was measured at end diastole as the ratio of 2 × posterior wall thickness/LV diameter.[7] The LV mass index (LVMI) was calculated by dividing LV mass by body surface area (BSA) to adjust for body size. The cutoffs of 131 g/m^2 for men and 100 g/m^2 for women developed in the Framingham Heart Study were used to define the presence of LVH.[1] A partition value of 45% for RWT was used for both men and women.[7] Four patterns of LV geometry were defined according to values of LVMI and RWT: normal (normal LV mass and RWT), concentric remodeling (normal LV mass and increased RWT), eccentric LVH (increased LV mass and normal RWT), and concentric LVH (increased LV mass and RWT).

Normal geometry, concentric remodeling, eccentric and concentric LVH were found in 47, 3, 13, and 9 subjects, respectively. At first, the subjects were classified into two groups according to the presence LVH. Patients with LVH were then subdivided into eccentric and concentric LVH groups. Patients with concentric remodeling were excluded from the statistical analysis because of their limited number.

A Statistica 5.0 (StatSoft, Inc., Singapore) software was used for the statistics. Data are expressed as mean ± standard deviation (SD). Mann-Whitney-U and Student's *t*-tests for independent samples were employed to compare the ^{99m}Tc sestamibi c/m ratio and echocardiographic parameters between the groups. Student's *t*-test for dependent samples was used to estimate the inter- and intraobserver variabilities. The correlations between scintigraphic and echocardiographic variables were assessed by using the multiple linear regression analysis and Pearson's r coefficient. Significance was set at a p value of < 0.05.

Results

Two groups with normal geometry and LVH were comparable in age and gender distribution (48 ± 11 years, 25 men/25 women; 50 ± 15 years, 10 men/12 women, respectively). Table I shows the echocardiographic and hemodynamic parameters of the subjects and the comparison of these parameters between the normal geometry and LVH groups. Table II displays the comparison of these parameters between the concentric and eccentric LVH groups.

TABLE I Echocardiographic and hemodynamic parameters of the study group

	Normal geometry	LVH	p Value
LVEDD (cm)	4.9 ± 0.4	5.3 ± 0.4	0.0001
IVST (cm)	0.87 ± 0.13	1.17 ± 0.25	0.0001
PWTd (cm)	0.75 ± 0.13	1.09 ± 0.26	0.0001
RWT (%)	30 ± 5	40 ± 10	0.0001
LVMI (g/m^2)	87 ± 24	176 ± 58	0.0001
EDV (ml)	119 ± 26	152 ± 35	0.0001
ESV (ml)	60 ± 58	77 ± 44	NS
SV (ml)	68 ± 19	91 ± 31	0.001
LVEF (%)	56 ± 10	60 ± 10	NS
FS (%)	29 ± 8	26 ± 13	NS
SBP (mmHg)	128 ± 24	152 ± 30	0.001
DBP (mmHg)	79 ± 13	91 ± 18	0.01

Abbreviations: LVH = left ventricular hypertrophy, LVEDD = left ventricular end-diastolic dimension, IVST = interventricular septal thickness, PWTd = diastolic posterior wall thickness, RWT = relative wall thickness, EDV = end-diastolic volume, ESV = end-systolic volume, SV = stroke volume, LVEF = left ventricular ejection fraction, FS = fractional shortening, LVMI = left ventricular mass index, SBP = systolic blood pressure, DBP = diastolic blood pressure, NS = no significant difference.

TABLE II Comparison of echocardiographic and hemodynamic parameters between concentric and eccentric left ventricular hypertrophy groups

	Eccentric LVH	Concentric LVH	p Value
LVEDD (cm)	5.5 ± 0.4	5.1 ± 0.3	NS
IVST (cm)	1.05 ± 0.17	1.3 ± 0.2	0.01
PWTd (cm)	0.94 ± 0.18	1.2 ± 0.2	0.001
RWT (%)	34 ± 5	50 ± 6	0.001
LVMI (g/m^2)	150 ± 32	205 ± 76	NS
EDV (ml)	162 ± 38	136 ± 30	NS
ESV (ml)	65 ± 24	96 ± 43	NS
SV (ml)	97 ± 26	87 ± 28	NS
LVEF (%)	58 ± 9	61 ± 12	NS
FS (%)	25 ± 13	31 ± 7	NS
SBP (mmHg)	159 ± 24	157 ± 35	NS
DBP (mmHg)	92 ± 14	94 ± 21	NS

Abbreviations as in Table I.

Significantly decreased c/m ratio was found in patients with LVH compared with subjects with normal geometry (0.05 ± 0.02 vs. 0.17 ± 0.08, p = 0.001). The ± 95% confidence interval of the c/m ratio for patients with normal geometry was 0.124 to 0.256. The ability of a c/m ratio < 0.124 to identify patients with LVH is presented in Table III. A c/m ratio < 0.124 correctly identified 19 of 22 patients with LVH; the remaining 3 patient had a mean LVMI of 111 ± 8 g/m^2 (ranges 106–122 g/m^2), all of which being eccentric LVH. A c/m ratio > 0.124 correctly detected normal geometry in 30 of 47 subjects; and the mean LVMI of remaining 17 had a mean LVMI of 92 ± 24 g/m^2. When a c/m ratio of 0.124 was accepted as the cut-off value, a c/m ratio of < 0.124 yielded a sensitivity of 86%, a specificity of 64%, and an overall diagnostic accuracy of 68% for detecting LVH in patients free of myocardial ischemia.

When concentric and eccentric LVH groups were separately compared with the normal group, both LVH groups showed significantly lower values of c/m (0.07 ± 0.02 and 0.02 ± 0.01, p = 0.01 for both) (Table IV). However, the c/m ratio was not significantly different between the two patterns of LVH.

Negative correlations of the c/m ratio were found to LVMI (r = −0.41, p = 0.0001), LV end-diastolic dimension (r = −0.37, p = 0.01), septal width (r = −0.42, p = 0.01), posterior wall thickness (r = −0.39, p = 0.001), RWT (r = −0.40, p = 0.001), and end-diastolic volume (EDV) (r = −0.41, p = 0.0001). The potentials of LVMI, ejection fraction, and EDV in predicting c/m ratio were assessed by standard-mode multiple linear regression analysis. The LVMI was the single independent predictor of c/m ratio. The regression equation of c/m ratio was [^{99m}Tc sestamibi c/m = 0.346 − (0.00077 × LVMI) (R = 0.48, F (2.58) = 8.56, p = 0.0005)].

Discussion

The activity and count density of myocardial perfusion SPECT agents within the LV cavity has been a subject of a few studies that were primarily focused upon LV function.[8–12] Decreased c/m ratio calculated both from 201-thallium[8,9] and ^{99m}Tc sestamibi[10–12] images was suggested as a parameter reflecting poor LV function. We hypothesized that increased myocardial wall thickening would result in an increased level of myocardial count density and subsequent decreased levels of c/m, and LVH could that way be diagnosed by ^{99m}Tc sestamibi imaging.

The underlying scenario of decreased c/m ratio in both eccentric and concentric LVH needs to be clarified. Although the difference between two LVH patterns reached no statistical significance, patients with concentric LVH had the lowest mean level of c/m ratio among the groups. This finding can simply be linked to the predominantly increased wall thickness against a normal LV cavity dimension in the definition of concentric pattern. Therefore, a statistically significant difference between concentric and eccentric LVH could conceivably be expected in larger cohorts.

The mechanism of decreased c/m ratio in eccentric pattern, however, should be interpreted in a different manner since these patients have predominantly increased LV cavity dimension. In our opinion, decreased c/m ratio in these patients could be explained with decreased ^{99m}Tc sestamibi activity in the enlarged LV cavity. A few previous observations suggested that LV cavities of failing hearts appear to have decreased tracer activity.[8–10] That was explained by decreased spillover activity of failing myocardium into the cavity due to limited movement of myocardial walls.[8–11] Normally, the level of tracer activity within the cavity is most likely due to the activity in the myocardium rather than that in the blood pool.[8] Decreased c/m ra-

TABLE III Diagnostic accuracy of c/m ratio for detecting left ventricular hypertrophy

	LVH	Normal geometry	
C/m ratio < 0.124	19	17	X^2 = 15.13
C/m ratio > 0.124	3	30	p = 0.0001

Sensitivity of c/m ratio for left ventricular hypertrophy (LVH): 86%. Specificity of c/m ratio for LVH: 64%. Overall diagnostic accuracy: 68%.

TABLE IV Comparison of c/m ratio between normal geometry and concentric and eccentric left ventricular hypertrophy groups

C/m ratio	Normal geometry	Eccentric LVH [a]	Concentric LVH [a]
Mean	0.17	0.07	0.02
Standard deviation	0.08	0.02	0.01

[a] p ≤ 0.01. The p values were calculated for comparison of the data for both LVH subgroups with the normal geometry.

tio could be explained with a mechanism that the eccentric LVH has a larger cavity receiving the same amount of spillover activity from the surrounding myocardium.[8–11] Therefore, our eccentric LVH group with normal LV functions and failing hearts of other studies share a similar mechanism explaining decreased c/m ratios.

Limitations of the Study

The major limitation of the study was the small size subgroups that might have resulted in a failure to differentiate further the specific LV geometric patterns by which we subclassified our patients; thus, the potential significance in the discriminative power of the c/m ratio between those patterns might have been obscured. Furthermore, the value of the index seems to be limited to patients free of any LV contractile dysfunction where a similar decrease in c/m ratio, as mentioned above, could be observed.

Since the study was retrospectively conducted on the images obtained from patients in whom stress perfusion imaging revealed no ischemia, no rest perfusion image was further required in any of those patients during their examinations; therefore rest images were not available at the time our work was performed. Considering less variable blood flow and myocardial activity concentrations at rest, the acquisition of scintigraphic data from DS was a study limitation. We presume that future investigations utilizing rest perfusion images would be of particular interest in demonstrating the potential value of the index in discriminating LVH from normal geometry in patients without and with coronary artery disease as well. Finally, gated image acquisition performed in the majority of current SPECT myocardial perfusion studies would be more appropriate for delineating the c/m ratios.

Conclusion

A new scintigraphic index, c/m ratio obtained from ^{99m}Tc sestamibi SPECT images, has a potential in detecting LVH in patients without myocardial ischemia. This interesting issue warrants further investigation, and future studies are required to clarify the value of this parameter in different study groups, particularly in patients with scintigraphically detected ischemia and infarction, and its ability to predict prognosis.

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