Thallium-201 Single-Photon Emission Computed Tomography: Quantitative Assessment of Left Ventricular Perfusion and Structural Change in Patients with Chronic Aortic Regurgitation

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Summary

Background: Previously, perfusion defect in the left ventricle was detected by thallium-201 (^{201}Tl) single-photon emission computed tomography (SPECT) in aortic regurgitation (AR). The significance of ^{201}Tl SPECT, however, has not been clarified. Limited information is available regarding the relationship between functional characteristics and scintigraphic findings.

Hypothesis: The purpose of this study was to elucidate the role of exercise ^{201}Tl SPECT in assessing myocardial perfusion or structural change in chronic AR. We examined the correlation between ^{201}Tl scintigraphic findings and left ventricular (LV) function parameters in 11 patients.

Methods: Defect volume ratio (DVR) in exercise ^{201}Tl SPECT was used as a parameter of the range of abnormal thallium distribution. Left ventricular parameters were obtained by right and retrograde left cardiac catheterizations. The relationship between DVR and the parameters was analyzed.

Results: The DVR ranged from 1.0 to 28.3% (average $12.1 \pm 8.5\%$). There was a significant correlation ($r = 0.77$, $p < 0.05$) between DVR and end-diastolic volume index (EDVI), a definite correlation ($r = 0.66$, $p < 0.01$) between DVR and end-systolic volume index (ESVI), and a good correlation ($r = -0.77$, $p < 0.05$) between DVR and end-systolic wall stress (ESS)/ESVI; however, no such correlation was found between DVR and ejection fraction.

Conclusion: All patients showed abnormal defects in ^{201}Tl accumulation scattered across the entire ventricle. A strong correlation between DVR and ESS/ESVI, an index of myocardial contractility, was a major finding of this study, suggesting a significant association between abnormal myocardial perfusion or structural alteration and reduction in myocardial contractility in chronic AR.

Key words: single-photon emission computed tomography, aortic regurgitation, left ventricular function

Introduction

Some patients with chronic aortic regurgitation (AR) show poor functional response to aortic valve replacement and are at a high risk of dying postoperatively, either suddenly or from congestive heart failure.^{1,2} It has been suggested that the underlying cause of poor outcome is excessive cellular hypertrophy and interstitial fibrosis preoperatively. Previous studies have reported that structural change in the endocardium, especially interstitial fibrosis, is associated with myocardial contractile dysfunction and is therefore of prognostic value in the disease.^{3,4}

Recent progress in myocardial scintigraphic analysis allows for noninvasive assessment of myocardial perfusion or viability. In chronic AR, thallium-201 (^{201}Tl) scintigraphy often reveals imaging defects representing abnormal myocardial perfusion of the left ventricle, although the coronary arteriograms are normal.^{5,6} However, limited information is available regarding the relationship between functional characteristics and scintigraphic findings of the myocardium.

The purpose of this study was to elucidate the role of exercise ^{201}Tl single-photon emission computed tomography (SPECT) in assessing myocardial perfusion or structural change in patients with chronic AR. We examined the correlation between ^{201}Tl scintigraphic findings and parameters of left ventricular (LV) function.

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Methods

Subjects

Eleven consecutive patients (6 men, 5 women) with a mean age of 58 ± 8 years (range 22–75 years), who had isolated, chronic AR and had undergone cardiac catheterization, participated in this study. They underwent ^{201}Tl SPECT during supine exercise on bicycle ergometer. Their clinical characteristics are shown in Table I. Five patients were asymptomatic, five were minimally symptomatic (functional class II of the New York Heart Association), and one was severely symptomatic (class III).

Cardiac Catheterization

Right and retrograde left cardiac catheterizations were performed in all patients. Left ventriculogram was performed as described previously.¹ Cardiac volume was obtained from right anterior oblique ventriculograms. Volumes were calculated by area-length method and corrected by the regression equation derived by Wynn *et al.*⁷ End-systolic volume (ESV) and end-diastolic volume (EDV) were defined as the smallest and largest ventricular volumes, respectively, as identified from serial frames. Ejection fraction (EF) was calculated as $(\text{EDV} - \text{ESV})/\text{EDV}$. Left ventricular mass was determined at end-diastole by the method of Rackley *et al.*⁸ Myocardial wall thickness was measured in the middle third of the anterior wall in the right anterior oblique view of the end-diastolic frame.⁹ Volumes and mass were indexed for body surface area. End-systolic circumferential wall stress (ESS) was calculated using Mirsky's formula.¹⁰ The ratio of ESS to ESV was calculated as a measure of myocardial contractility.

Exercise Thallium-201 Single-Photon Emission Computed Tomography

All patients were studied in supine position and asked to perform supine bicycle exercise at an initial load of 25 W, with increments of 25 W every 3 min. The exercise test was terminated if the patient complained of chest pain, leg fatigue, general fatigue, shortness of breath, and so forth, or if significant ST-segment elevation or depression was observed on electrocardiographic (ECG) monitor, or the heart rate reached 85% of the maximal target heart rate. During exercise, ^{201}Tl was injected, following which the patients exercised for one more minute. The SPECT image was taken 10 min after the injection. A single crystal scintillation camera, equipped with a high sensitivity, parallel-hole collimator, interfaced to an on-line computer system (harmonic phase [HARP]) was used. The detector was positioned on the chest wall of each patient in a 30° to 50° left anterior oblique projection with a 5° to 10° caudal tilt; the angulation was adjusted so that the image of the left ventricle was clearly separated from that of the right ventricle and the left atrium. Using the slice with the greatest cavity length, the operator selected the apex and long axis of the left ventricle. Using the long axis, the image of the left ventri-

TABLE I Clinical characteristics of patients

No.	Age	Sex	AR grade	NYHA	CTR (%)
1	75	F	2	1	52
2	29	F	3	1	55
3	62	M	3	2	64
4	45	M	4	1	65
5	52	F	4	3	72
6	40	F	2	2	50
7	22	M	3	1	50
8	34	M	2	1	46
9	51	F	3	2	51
10	46	M	3	2	55
11	51	M	4	2	56

Abbreviations: AR = aortic regurgitation, NYHA = New York Heart Association, CTR = cardiothoracic ratio, F = female, M = male.

cle was divided into 16 short axial slices and the center point of the LV cavity was defined. The circumferential profile of each short axial slice was generated from the most basal to the most apical slice. Each point in these profiles represents the maximum counts per pixel along a radius that extends from the center point of the left ventricle to the limit of the radius search. Each radius was spaced at a 6° interval that was plotted counterclockwise, and each short axial slice was divided into 60 segments. The maximal counts per pixel along each radius were defined as the count of the segment between two consecutive radii. The maximum count in each segment was indexed for the maximum count of the slice (% profile).

Normal limits were defined in each segment as two standard deviations (SD) below the mean %profile, which was generated from 20 normal controls. The segments in which the %profile fell below the normal limits were considered to be defect segments (Fig. 1). After examination, all segments were expressed in a two-dimensional polar coordinate map (Fig. 2). The defect volume ratio (DVR), calculated using the

FIG. 1 Circumferential profile curve: maximum count in each segment was indexed for the maximum count of the slice (% profile) and plotted on each radiation. The segments where the % profile fell below normal limits were considered as defect segments (stripped area, Nn).

FIG. 2 All segments were mapped into a two-dimensional polar representation. In this map, the apex corresponds to the center of polar representation and the outermost circle corresponds to the most basal cut. The white region in the map corresponds to locations where circumferential profiles fell below normal limits.

formula in Figure 3, was used as a parameter of the range of abnormal thallium distribution. It represents the ratio of the myocardium with abnormal thallium distribution to the entire myocardium.¹¹

Statistics

Data are expressed as mean $\pm$ SD. Lower limit data for quantitative analysis of exercise ²⁰¹Tl SPECT were obtained from 20 normal subjects. The relationship between DVR and angiographic data was tested by linear regression analysis. A *p* value of ≤ 0.05 was considered significant.

TABLE II Hemodynamic data from catheterization and defect volume ratio

No.	EDVI	ESVI	ESS/ESVI	EF	DVR
1	82	21	7.4	74	3.08
2	158	81	3.9	48	17.49
3	148	48	3.9	68	4.17
4	171	81	3.1	53	13.73
5	199	111	2.0	44	22.24
6	97	34	^a	65	4.52
7	183	87	2.7	53	14.04
8	149	56	3.1	63	12.87
9	130	57	5.2	56	0.98
10	182	128	^a	30	12.00
11	185	87	^a	53	28.04
Mean $\pm$ SD	153 $\pm$ 37	72 $\pm$ 32	3.9 $\pm$ 1.7	55 $\pm$ 12	12.1 $\pm$ 8.5

^aData not available.

Abbreviations: EDVI = end-diastolic volume index, ESVI = end-systolic volume index, ESS = end-systolic wall stress, EF = ejection fraction, DVR = defect volume ratio, SD = standard deviation.

FIG. 3 (A) Formula for calculating defect volume ratio (DVR): the left ventricle was divided into 16 short axial slices. *Rn* = radius of slice, *h* = height of slice, *d* = depth of slice *n*. (B) Formula for calculating defect volume ratio (DVR): each short axial slice was divided into 60 segments.

$$DVR = \frac{\sum 2 \pi r_n \cdot N_n / 60 \cdot h \cdot d}{2 \pi r_n \cdot h \cdot d}$$

Results

Table II shows cardiac catheterization data and DVR assessed by exercise ²⁰¹Tl SPECT. A correlation was observed between DVR and the parameters of LV function (Table III).

Cardiac Catheterization Data

We observed that EDVI and ESVI of these patients were more elevated than those of normal subjects (153 $\pm$ 37 vs. 82 $\pm$ 13 ml/m², 72 $\pm$ 32 vs. 28 $\pm$ 7 ml/m²; *p* < 0.05), whereas ESS/ESVI and EF of these patients were lower than those of normal control (3.9 $\pm$ 1.7% vs. 17.2 $\pm$ 1.3%; 55 $\pm$ 12% vs. 67 $\pm$ 6%; *p* < 0.01, *p* < 0.05).

TABLE III Relation between defect volume ratio and angiographical index

	<i>r</i>	<i>p</i> Value
EDVI	0.77	<0.01
ESVI	0.66	<0.05
ESS/ESVI	-0.77	<0.05
EF	0.51	NS

Abbreviations as in Table II.

FIG. 4 Relationship between defect volume ratio (DVR) and end-diastolic volume index (EDVI).

Exercise Thallium-201 Single-Photon Emission Computed Tomography

The DVR ranged from 1.0 to 28.3%, with an average of $12.1 \pm 8.5\%$. All patients showed abnormal thallium distribution.

There was a significant correlation ($r = 0.77$, $p < 0.05$) between DVR and EDVI, and a definite correlation ($r = 0.66$, $p < 0.01$) was observed between DVR and ESVI. (Figs. 4, 5)

A good correlation ($r = -0.77$, $p < 0.05$) was observed between DVR and ESS/ESVI (Fig. 6); however, there was no such correlation between DVR and EF.

Discussion

The relationship between ^{201}Tl multiple defects and myocardial damage indicated by myocardial fibrosis on histopathology has been shown in dilated cardiomyopathy.^{12, 13} Several reports suggested that LV perfusion defect was detected by ^{201}Tl SPECT in AR;^{5, 6} however, the significance of ^{201}Tl defect image has not been clarified.

In this study, all patients had abnormal defects in ^{201}Tl accumulation, and the defect segments were scattered across the entire ventricle. A strong correlation between DVR and ESS/ESVI, an index of myocardial contractility, was a major finding of this preliminary study, suggesting a significant association between abnormal myocardial perfusion or structural al-

teration and reduction in myocardial contractility in chronic AR. Significant correlation between scintigraphic finding and LV volume was another important finding. In chronic AR, LV hypertrophy is an adaptive response to volume load, which in itself is a compensatory mechanism.^{14, 15} However, progressive dilatation leads to depressed left ventricle contractility and myocardial structural change with interstitial fibrosis.^{3, 4} Therefore, these findings indicate the importance of exercise ^{201}Tl SPECT in evaluating the structural remodeling and contractile dysfunction in ventricular hypertrophy.

Scintigraphy versus Biopsy

Myocardial damage has been conventionally evaluated by histopathologic changes in endomyocardial biopsy specimen from cardiac catheterization.¹⁴ Several studies on the association between histopathologic changes and LV function in AR have shown a correlation between myocardial hypertrophy or interstitial fibrosis and impaired LV function.^{3, 4} These findings suggest that extensive cellular degeneration and increased interstitial fibrosis may be essential for causing the myocardial damage.

In conventional histopathologic evaluation by subendocardial biopsy, uniform myocardial changes in the entire left ventricle are prerequisites for assessing myocardial damage. Schwarz *et al.*¹⁵ demonstrated that a similar degree of fibrosis exists in endocardium and epicardium. Schoen *et al.*¹⁶ reported that morphologic changes in myocardium were uniformly distributed across the entire ventricle in aortic valve disease. Endocardial biopsy, as it is invasive technique, is considered to be a major drawback of histopathologic evaluation; conducting serial evaluation is difficult and expensive. On the other hand, scintigraphy is advantageous as it is less invasive or noninvasive.

A methodological difficulty faced during ^{201}Tl SPECT is that the size of each segment, as the minimum unit of analysis, is determined by its resolution and varies widely from the actual cell level. The evaluation is performed using the mean per unit segment. Unlike histopathologic findings, ^{201}Tl SPECT does not directly reveal cell degeneration or fibrosis; however, it allows assessment of the entire image.

FIG. 5 Relationship between defect volume ratio (DVR) and end-systolic volume index (ESVI).

FIG. 6 Relationship between defect volume ratio (DVR) and end-systolic wall stress / end-systolic volume index (ESS/ESVI).

Clinical Implications

In this study, all patients revealed abnormal ^{201}Tl distribution. An important finding is that DVR significantly correlated with the parameters of LV function. It is, therefore, justifiable to assume that DVR can be used for quantitative analysis of LV impairment. The defects may reflect the degree of structural change, that is, degeneration and fibrosis, and decrease in regional blood flow.

Serial evaluation of patients with AR can be conducted by exercise ^{201}Tl SPECT. Preoperative and postoperative evaluation could predict both late outcome and appropriate time for surgery.

Conclusion

Although the defect images in exercise ^{201}Tl SPECT may be affected by a relative decrease in coronary blood flow and does not directly represent histopathologic degeneration of myocardial cells, the structural change and relative ischemia can be simultaneously evaluated noninvasively. In addition, a good correlation between exercise ^{201}Tl SPECT findings and LV function suggests the usefulness of this method. The defect image could possibly be related to the progression of myocardial fibrosis due to chronic volume overload.

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