



# Assessment of Left Ventricular Function Using Dobutamine Stress Echocardiography and Myocardial Scintigraphy in Valvular Heart Disease

Ozaki, Nobuchika  
Sugimoto, Takaki  
Okada, Masayoshi

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ASSESSMENT OF LEFT VENTRICULAR FUNCTION USING  
DOBUTAMINE STRESS ECHOCARDIOGRAPHY AND  
MYOCARDIAL SCINTIGRAPHY IN VALVULAR HEART DISEASE

Nobuchika OZAKI, Takaki SUGIMOTO, and Masayoshi OKADA

Second Division, Department of Surgery, Kobe University School of Medicine

**INDEXING WORDS**

valvular heart disease; left ventricular dysfunction; dobutamine stress echocardiography; myocardial scintigraphy

**SYNOPSIS**

To assess the left ventricular (LV) function in valvular heart disease, we employed the preoperative dobutamine stress echocardiography and the myocardial scintigraphy. During the past 13 years, 37 of 324 the patients showed LV dysfunction with the % fractional shortening (%FS) of 25% or less in the preoperative echocardiogram. These patients were retrospectively divided into two groups; Group A (n=21) : %FS has improved late after operation; Group B (n=16) : %FS has deteriorated or LV failure occurred. The mean follow-up period was  $84 \pm 54$  months after valve surgery. No significant differences were observed in the preoperative characteristics and operative variables between these two groups. The dobutamine stress test had been performed in 8 patients in Group A and 9 patients in Group B preoperatively, and the maximum increase ratio of %FS ( $\Delta$  %FS) was used for assessment. Seven patients in Group A had showed  $\Delta$  %FS of more than 9%, while all patients in Group B had showed  $\Delta$  %FS of less than 9%. Myocardial scintigraphy was performed in 11 patients of them, and another 22 patients with %FS of above 25% acted as the control group. The Defect Score, which was defined as the sum of defect scales in 25 LV segments, showed a significant difference between 11 patients with LV dysfunction and control group. The distribution of the Defect Score in each myocardial segment, showed significantly higher in the posterior and inferior LV segments. In addition, the perfusion defect on myocardial imaging was initiated in the junction between the septal and LV free wall, and extended from the posterior to the lateral wall along with deterioration of LV function. In conclusion, preoperative dobutamine stress echocardiography proved to be very useful for prediction of the postoperative LV function, and myocardial scintigraphy might be indicative of LV function even in valvular heart disease.

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Authors' names in Japanese : 尾崎喜就、杉本貴樹、岡田昌義

## INTRODUCTION

Surgical outcome of valvular heart disease has improved with improvement of myocardial protection and surgical procedures, and patients with left ventricular (LV) dysfunction have been also candidates for surgical intervention. However, it has been still difficult to predict the postoperative behaviors of LV function especially in patients with LV dysfunction. In this paper, we assessed LV function using dobutamine stress echocardiography and myocardial scintigraphy.

## MATERIALS AND METHODS

Between January 1984 and December 1997, 324 patients underwent cardiac valve operations in Kobe university hospital. Among them, 37 patients had no coronary artery lesion and showed % fractional shortening (%FS) of 25% or less in the preoperative echocardiogram. They consisted of 20 males and 17 females, ranging in age from 32 to 71 years (mean,  $51 \pm 8.7$  years). Aortic stenosis with regurgitation (ASR) was in two patients, aortic stenosis (AS) in two, aortic regurgitation (AR) in six, mitral stenosis with regurgitation (MSR) in two, mitral stenosis (MS) in 15, mitral regurgitation (MR) in two, AR and MR in three, AR and MS in four, and AS and MS in one. As operations, aortic valve replacement (AVR) was performed in 10 patients, mitral valve replacement (MVR) in 19, and AVR and MVR in eight. All patients underwent the preoperative echocardiography within one week before operation in hemodynamic stability, and 17 of them underwent dobutamine stress test at the same time (Table I). The dobutamine stress test was performed as follows. Dobutamine was infused at 3, 6, and  $9 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ , with a 5-minute interval for each dose. The increase ratio of %FS at the maximum point of LV contraction was defined as  $\Delta\%$ FS. The postoperative echocardiography was performed one month after operation, and thereafter every 6 months. The follow-up period ranged from 9 to 163 months ( $84 \pm 54$  months). All patients have been followed now with good repair of the valvular lesions. None have undergone a redo surgery. Good repairs of the valve lesions were confirmed with Doppler echocardiographic examination which showed a functional mitral orifice area of above  $2.5 \text{ cm}^2$  and pressure gradient across the aortic valve of below 30 mmHg with no perivalvular regurgitation.

These patients were retrospectively divided into two groups; Group A (n=21): %FS has gradually improved late postoperatively; Group B (n=16): %FS has deteriorated late postoperatively. Group B included three patients who died of LV failure (Fig.1). The preoperative dobutamine stress echocardiography had been performed in 8 patients in Group A and 9 patients in Group B.

### *Myocardial Scintigraphy*

Myocardial scintigraphics were carried out in 11 patients with LV dysfunction, and another 22 patients with %FS of above 25% acted as the control group. All patients had no coronary

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artery lesions. They consisted of 21 males and 12 females, ranging in age from 34 to 75 years (mean,  $58 \pm 9.8$  years). The valve lesions were as follows: ASR in one; AS in four; AR in seven; MSR in two; MS in four; MR in twelve; AR and MR in two; and AS and MS in one. All patients underwent thallium (Tl) -201 or technetium (Tc) -99m sestamibi (MIBI) or Tc-99m tetrofosmin single photon emission computed tomographic study (SPECT), and 17 patients including 12 patients of control group underwent iodine-123 (123I) - iodophenylpentadecanoic acid (BMIPP) SPECT. Scintigraphic data was scored by two independent observers blinded to the echocardiographic data. The left ventricle was divided into 25 segments, and each segment was graded on a 4-point defect scale: 0, normal; 1, mild hypoperfusion; 2, moderate hypoperfusion; 3, severe hypoperfusion or defect. The sum of the scales was defined as the Defect Score.

### *Statistical Analysis*

All data were expressed as mean  $\pm$  standard deviation. Demographic variables were compared between patient groups by Student's t test or  $\chi^2$  testing as appropriate. The changes in %FS from the preoperative to the postoperative period were compared with a paired t test. A value of  $P < .05$  was considered significant.

Table I. Valvular Heart Diseases with Left Ventricular Dysfunction.

	Group A (Dobutamine stress test)		Group B (Dobutamine stress test)		all	
ASR	1	(0)	1	(1)	2	(1)
AS	0	(0)	2	(1)	2	(1)
AR	2	(1)	4	(2)	6	(3)
MSR	2	(0)	0	(0)	2	(0)
MS	10	(5)	5	(2)	15	(7)
MR	2	(2)	0	(0)	2	(2)
AR+MR	1	(0)	2	(1)	3	(1)
AR+MS	2	(0)	2	(2)	4	(2)
AS+MS	1	(0)	0	(0)	1	(0)
	21	(8)	16	(9)	37	(17)

ASR indicates aortic stenosis and regurgitation; AS, aortic stenosis; AR, aortic regurgitation; MSR, mitral stenosis and regurgitation; MS, mitral stenosis; MR, mitral regurgitation

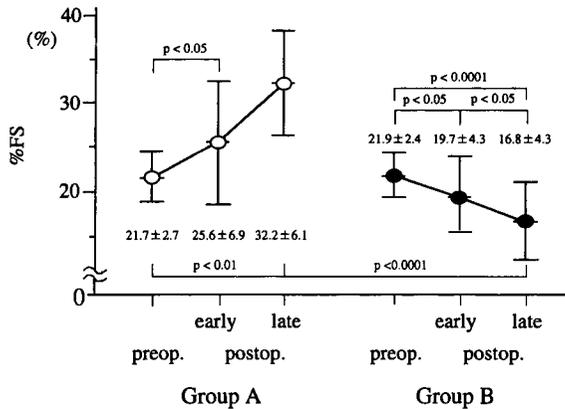


Fig. 1. Serial changes of %FS in two groups. In Group A, %FS improved early postoperatively and much more late postoperatively. In Group B, %FS regressed gradually.

RESULTS

The preoperative baseline characteristics and operative variables are summarized in Table II. No significant differences were seen in gender, age, New York Heart Association (NYHA) functional class, LV dimension at end-diastole (Dd), dimension at end-systole (Ds), %FS, operative frequency, extracorporeal circulation (ECC) time, and aortic cross clamp (ACC) time between Group A and Group B, as well as in dobutamine stress test cases (Table II). In contrast, 7 of 8 patients in Group A had showed a Δ %FS of 9% or greater, while all of 9 patients in Group B had showed a Δ %FS of 9% or less in dobutamine stress test. A distinct difference was seen between Group A and Group B (Fig.2).

Table II. Comparisons of Preoperative and Operative Variables between Group A and Group B.

	Group A	(Dobutamine stress test)	Group B	(Dobutamine stress test)	p-value
GENDER	♂ 11, ♀ 10	(♂ 7, ♀ 1)	♂ 9, ♀ 7	(♂ 4, ♀ 5)	N.S. (N.S.)
AGE (yrs.)	51.3 ± 10.3	(49.5 ± 7.8)	51.7 ± 6.4	(53.7 ± 6.1)	N.S. (N.S.)
NYHA (class)	2.2 ± 0.7	(2.2 ± 0.8)	2.1 ± 0.6	(2.1 ± 0.4)	N.S. (N.S.)
Dd (mm)	56 ± 10.7	(56 ± 8.1)	63 ± 11.2	(63 ± 13)	N.S. (N.S.)
Ds (mm)	44 ± 9.2	(44 ± 8.0)	49 ± 9.1	(49 ± 11)	N.S. (N.S.)
%FS (%)	22 ± 2.7	(20 ± 2.4)	22 ± 2.4	(21 ± 2.3)	N.S. (N.S.)
op. freq.	1.5 ± 0.9	(2.0 ± 1.2)	1.6 ± 1.0	(1.8 ± 1.3)	N.S. (N.S.)
ECC (min.)	175 ± 71.0	(163 ± 45.6)	215 ± 141	(251 ± 181)	N.S. (N.S.)
ACC (min.)	104 ± 43.4	(94.5 ± 35.2)	114 ± 48.4	(115 ± 62.1)	N.S. (N.S.)

NYHA indicates New York Heart Association cardiac functional class; Dd, dimension of diastole; Ds, dimension of systole; %FS, %fractional shortening; op. freq, frequency of operation; ECC, extracorporeal circulation; ACC, aortic cross clamp; Group A (n=21): %FS has improved late postoperatively; Group B (n=16): %FS has deteriorated late postoperatively; N.S., not significant

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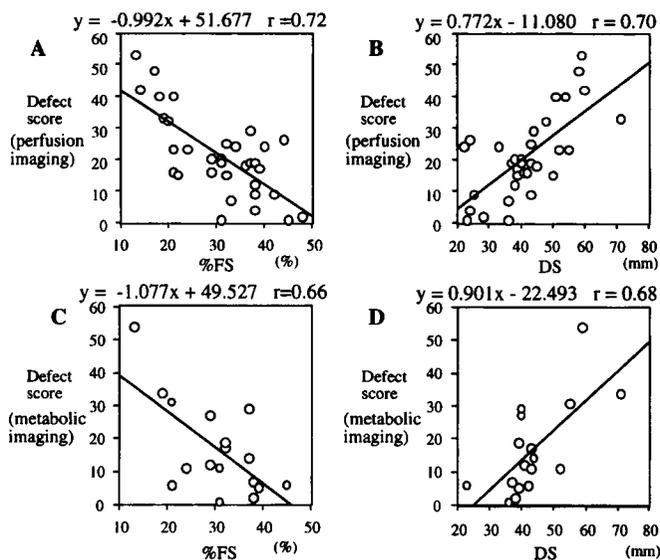


Fig. 4. Relationships between Defect score and %FS and DS. Defect score for myocardial perfusion imaging was significantly correlated with %FS (A) and Ds (B) in echocardiogram ( $r=.72$ ,  $r=.70$ , respectively) . Defect score for metabolic imaging was significantly correlated with %FS (C) and Ds (D) in left ventriculography ( $r=.66$ ,  $r=.68$ , respectively) .

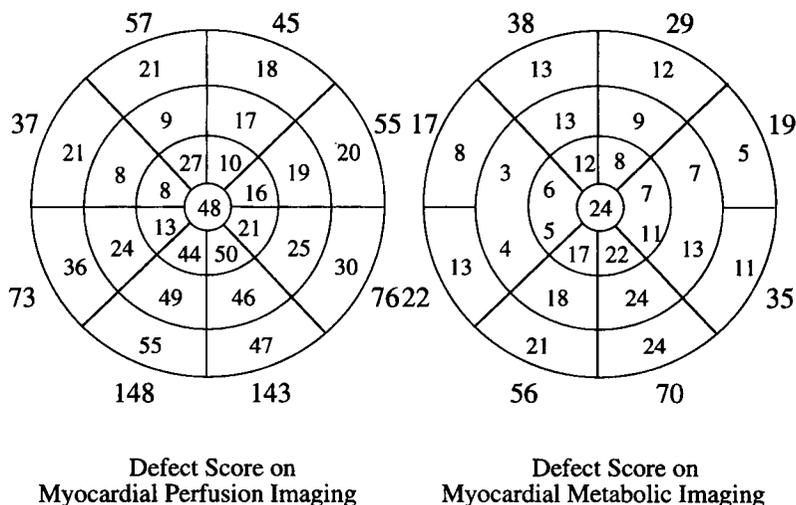


Fig. 5. Distribution of Defect score in each segment of left ventricle for myocardial perfusion and metabolic imaging. The sum of DS was significantly higher in the posterior and inferior segments than the other segments.

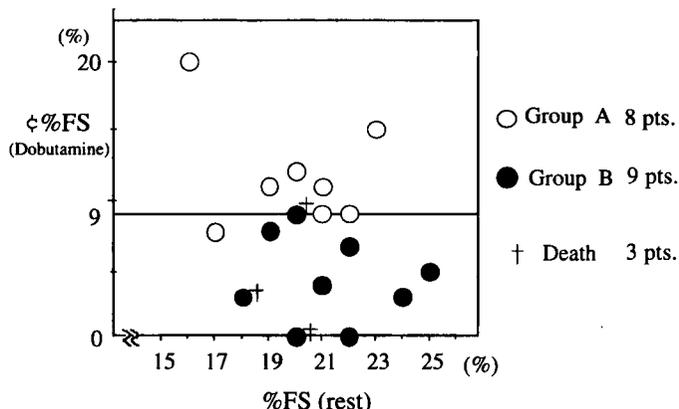


Fig. 2. Comparisons of %FS at rest and  $\Delta$  %FS in dobutamine stress echocardiography to postoperative LV function. Seven of 8 patients in Group A had  $\Delta$  %FS  $\geq$  9% and all patients in Group B had  $\Delta$  %FS < 9%.

In myocardial perfusion SPECT imaging with Tl-201 or Tc-99m (MIBI or tetrofosmin), the Defect Score ranges from 15 to 53 (mean,  $33 \pm 13$ ) in 11 patients with LV dysfunction and 1 to 29 (mean,  $15 \pm 8.5$ ) in control group. Significant differences were seen between these two groups ( $P < .0001$ ). In myocardial metabolic SPECT imaging with  $^{123}\text{I}$ -BMIPP, the Defect Score ranged from 6 to 54 (mean,  $27 \pm 19$ ) in 11 patients with LV dysfunction group, and 1 to 29 (mean,  $13 \pm 9.2$ ) in control group. There were also significant differences ( $P < .05$ ) between these two groups (Fig.3). In addition, the Defect Score in myocardial perfusion imaging and metabolic imaging were well correlated with %FS ( $r = .72, 0.66$ ) and Ds ( $r = .70, 0.68$ ) in echocardiogram, respectively (Fig.4). The distribution of the Defect Score in each LV segment showed significantly higher in the posterior and inferior segments (Fig.5). In addition, the perfusion defect on myocardial imaging was initiated in the junction between septal and LV free wall, and extended from the posterior to the lateral wall along with deterioration of LV function (Fig.6).

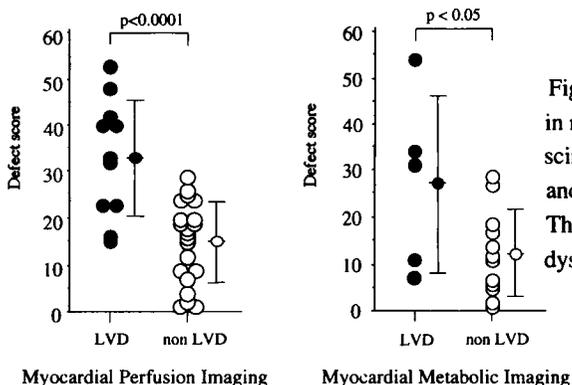


Fig. 3. Comparisons of Defect Score in myocardial perfusion and metabolic scintigrams between LV dysfunction and non LV dysfunction group. The DS was significantly higher in LV dysfunction group in both scintigrams.

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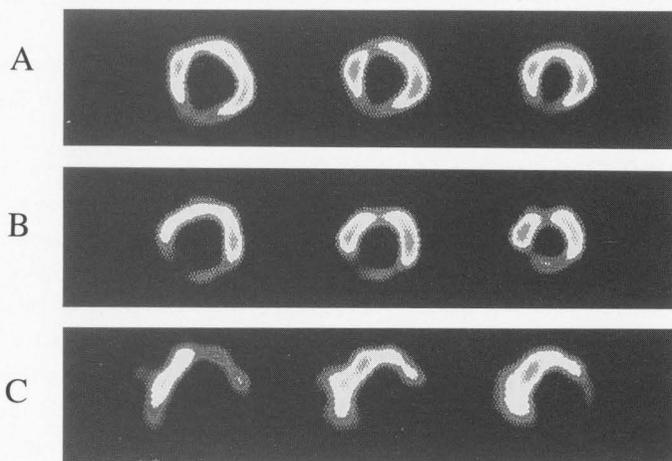


Fig. 6. Myocardial perfusion single photon emission computed tomography (SPECT) in the short axis at the basal, mid, and near apex portion. (A) This case had %FS of 21%,  $\Delta$  %FS>9% in dobutamine stress test, and Defect score of 16 for Tc-99m sestamibi imaging. (B) This case had %FS of 20%,  $\Delta$  %FS>9% in dobutamine stress test, and Defect score of 32 in 201Tl imaging. (C) This case had %FS of 17%,  $\Delta$  %FS<9% in dobutamine stress test, and Defect score of 48 in thallium-201 (201Tl) SPECT imaging. The perfusion defect initiated in the junction between septal and LV free wall, and extended from posterior to lateral wall along with deterioration of LV function.

### DISCUSSION

Regarding valvular heart disease, some studies were reported on postoperative prognosis of LV function in respective valve lesion<sup>1, 4, 9</sup>) as well as our previous studies.<sup>6, 11, 12</sup>) In this paper, we assessed LV function from viewpoint of the fact that deterioration of LV function finally causes the decrease of myocardial reserve faculty.

Various compensatory mechanisms work to LV load in valvular heart disease, and the relationship between load stress and compensatory mechanisms is maintained to some extent. However, the myocardium is gradually injured in this process. Although each myocyte grows in size, the number of myocytes does not markedly increase and capillaries do not grow around each myocyte. Consequently, ischemia appears in myocytes, and fibrosis is progressing in myocardial interstitium. With progression of interstitial fibrosis, LV compliance declines, and disturbance of its diastolic function reduces coronary blood flow, and causes ischemia. Thus, the myocardial

metabolism changes from fatty acid to glucose with deterioration of LV function.

Dobutamine stress echocardiography assesses the response to the adrenergic stimulus, and the positive inotropic response is considered to indicate myocardial viability.

Although we used %FS as an index of LV function, in this paper it is apt to be dependent on LV preload and afterload. Therefore, decrease of %FS is not always equal to the impairment of LV function.

In the setting of mitral stenosis, LV preload is limited and %FS indicates a lower value than the actual myocardial ability. Dobutamine stress increases LV contractility leading to decrease of LVDs. Therefore,  $\Delta$  %FS shows a higher value. In mitral regurgitation, LV contractility are in hyperdynamic state with increase of LV preload, and their %FS demonstrates higher values than actual myocardial condition. Dobutamine stress test reduced LVDs while LVDd maintained, therefore  $\Delta$  %FS is dependent on myocardial reserve faculty. In aortic stenosis, LV contraction is injured by increase of LV pressure afterload and %FS shows a lower value than the actual myocardial condition. In dobutamine stress test, LVDs and  $\Delta$  %FS is dependent on myocardial reserve faculty. In aortic regurgitation, LV preload increases, and %FS shows high values than actual myocardial condition. In dobutamine stress test, LV afterload slightly decreases and LV contractility increases. Therefore,  $\Delta$  %FS is dependent on LV afterload and myocardial ability.

Accordingly, %FS at rest is reflected by LV preload and afterload and  $\Delta$  %FS is influenced by response of LV myocardium to dobutamine. That is, patients with preservation of LV myocardial faculty shows good response to dobutamine irrespective of kinds of valvular disease. Although  $\Delta$  %FS is reflected by LV preload and afterload as well as %FS, it is mostly influenced by degree of LV myocardial impairment in patients with LV dysfunction. This paper showed a definite difference of postoperative behavior of LV contractility in the borderline of  $\Delta$  %FS of 9%. Thus the patients with  $\Delta$  %FS of more than 9% might possess enough myocardial faculty.

It is widely accepted that myocardial scintigraphy is very useful to evaluate ischemic heart disease or cardiomyopathy.<sup>3,8,10)</sup> In the present study, the relationship between scintigraphic abnormality and LV function and the locality of scintigraphic defect was investigated. The photon uptakes on myocardial perfusion and metabolic scintigram decreased with deterioration of LV function. That is, the Defect Score showed higher values in patients with LV dysfunction even in valvular heart disease. This indicates that LV myocardial factor itself greatly takes part in cardiac function. In addition, the perfusion defect on myocardial imaging initiated in the junction between septal and LV free wall, and extended from posterior to lateral wall along with deterioration of LV function. Myocardial disarray is considered to be present in this junction even in normal hearts.<sup>5,7)</sup> In addition, in ischemic and hypertrophic cardiomyopathy, myocardial fibrosis is found remarkably in this junction.<sup>5,7)</sup> Myocardial disarray and fibrosis might disturbed transmission of electrical activation and synchronous muscle contraction.<sup>2)</sup> The decrease of photon uptakes in this junction might indicate myocardial fibrosis. Therefore, myocardial fibrosis might be initiated in this junction and extended from posterior to lateral wall along with LV dysfunction in valvular heart disease.

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### CONCLUSION

Preoperative dobutamine stress echocardiography proved to be very useful for prediction of the postoperative LV function, and myocardial scintigraphy might be indicative of LV function even in valvular heart disease.

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