Resting Ultrasonic Tissue Characterization and Dobutamine Stress Echocardiography for Prediction of Functional Recovery in Chronic Left Ventricular Ischemic Dysfunction

Hiroshi Honma, MD; Yoshiki Kusama, MD; Tsuyako Matsuzaki*;
Tadaaki Ohno, MD; Ryutarou Nishigaki, MD; Kazuo Munakata, MD;
Hiroshi Kishida, MD; Teruo Takano, MD

This study was designed to assess the diagnostic accuracy of the percentage of resting systolic wall thickening (WT), dobutamine stress echocardiography (DSE), resting cyclic variation of integrated backscatter (IBS-CV), and low-dose dobutamine stress IBS-CV (DSE-IB) for the prediction of regional function recovery (RFR) in patients with chronic left ventricular (LV) ischemic dysfunction. The study also evaluated whether or not global LV function affected the diagnostic accuracy. All studies were conducted before percutaneous transluminal coronary angioplasty (PTCA) and RFR was assessed after PTCA (mean interval, 10 months) in 30 patients with chronic LV ischemic dysfunction. Patients were divided into 2 groups according to the LV ejection fraction (LVEF): group A, LVEF <40%, n=14; group B, LVEF ≥40%, n=16. Of a total of 480 segments, 37 initially demonstrating akinetic wall motion before PTCA were analyzed. The wall motion of 24 of the 37 segments improved on visual analysis after PTCA. In the prediction of RFR, resting WT, DSE, resting IBS-CV and DSE-IB had sensitivities of 79%, 79%, 92% and 62%, and specificities of 54%, 84%, 83% and 69%, respectively. In particular, the resting IBS-CV in group A, as well as DSE, was an excellent predictor of RFR (sensitivity, 100%; specificity, 86%; vs sensitivity, 82%; specificity, 78%; respectively). Therefore, both resting IBS-CV and DSE are useful predictors for RFR in patients with chronic LV ischemic dysfunction. (*Jpn Circ J* 2001; 65: 381–388)

Key Words: Cyclic variation of integrated backscatter; Dobutamine stress echocardiography; Myocardial contraction; Myocardial infarction; Reperfusion

Previous studies have shown the usefulness of low-dose dobutamine stress echocardiography (DSE) for the assessment of viable myocardium and the prediction of functional recovery after revascularization in patients with chronic coronary disease^{1–8}. However, there were wide ranges of sensitivity, specificity, and accuracy (74–91%, 73–95%, and 73–91%, respectively) for prediction of reversible dysfunction, possibly because most studies included patients with various degrees of regional and global left ventricular (LV) function. In addition, more precise equipment may be required in order to obtain a satisfactory level of the accuracy with DSE.

Recently, a cardiac cycle-dependent variation of ultrasonic integrated backscatter (IBS-CV), which reflects intramural contractile performance and myocardial thickening^{9–12} has been anticipated as useful for assessing myocardial viability and predicting LV functional recovery in patients with reperfused acute myocardial infarction¹³. In the setting of acute myocardial infarction, the characteristic of salvageable myocardium was reversibility of the blunted amplitude of IBS-CV. Pasquet et al reported that resting IBS-CV closely paralleled contractile reserve in patients with chronic LV ischemic dysfunction¹⁴ but further study is required to elucidate several aspects of the usefulness of IBS. We have

gradually increased the number of opportunities for evaluating the pertinence of revascularization in patients with chronic LV ischemic dysfunction, and so we designed this study to determine the sensitivity, specificity, and accuracy of resting % systolic wall thickening (resting WT), resting IBS-CV, DSE, and low-dose dobutamine stress IBS-CV (DSE-IB) in predicting functional recovery in patients with chronic LV ischemic dysfunction, and we also evaluated the effect of global LV function on the accuracy of this study.

Methods

Study Population

We studied 48 patients with a previous (mean 9±5 months after the onset) myocardial infarction between June and December, 1998. For inclusion in the study, the following criteria needed to be fulfilled.

1. Previous myocardial infarction including at least one akinetic segment as demonstrated by transthoracic echocardiography.
2. A suitable acoustic window to allow DSE with IBS.
3. Clinical evidence of myocardial ischemia, and scheduling for percutaneous transluminal coronary angioplasty (PTCA).
4. No cardiac event during the follow-up period after revascularization.

All patients underwent combined low- and high-dose DSE with IBS and radionuclide ventriculography (RNV) before PTCA. For a mean of 10 months (range, 5–24 months) after PTCA, transthoracic echocardiography at rest and the IBS study were repeated. All patients gave

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First Department of Internal Medicine and *Department of Physiological Examination, Nippon Medical School, Tokyo, Japan

Mailing address: Hiroshi Honma, MD, First Department of Internal Medicine, Nippon Medical School, 1-1-5 Sendagi, Bunkyo-ku, Tokyo 113-8603, Japan

Fig 1. Representative cyclic variation curves of IBS were obtained in the normal anterior septal wall (upper curve) and the inferoposterior wall (lower curve) (A). Cyclic variation in the infarcted inferoposterior wall (lower curve) showed an asynchronous pattern (B). The schema shows the magnitude of IBS-CV and the delay of IBS-CV expressed as Y divided by the QT interval.

informed consent, and the study protocol was approved by the institutional ethical committee.

Cardiac Catheterization

Selective coronary arteriography and PTCA were performed from the femoral approach. The indications for PTCA were clinical evidence of ischemia and myocardial viability in the territory of any coronary artery with significant stenosis ($\geq 75\%$ reduction of luminal diameter).

Radionuclide Ventriculography

The global LV function, expressed as the LV ejection fraction (LVEF) was assessed by RNV at rest before and a mean of 10 months after PTCA.

Dobutamine Stress Echocardiography

All patients were permitted to continue all of their cardiac medication except for β -blockers, which were withdrawn 48 h before the DSE study. Transthoracic echocardiography at rest was performed with the patient in the left decubitus position using a SONOS 2500 with a 2.5-MHz transducer (Hewlett-Packard, Andover, MA, USA). The echocardiographic standard views (parasternal long axis, parasternal short axis at 2 levels, apical 4-chamber, apical 2-chamber, and apical long axis views) were obtained. The left ventricle was divided into 16 segments according to the recommendation of the American Society of Echocardiography.¹⁵ Segmental wall motion was scored as follows: 1 = normal, 2 = mildly hypokinetic, 3 = severely hypokinetic, 4 = akinetic, 5 = dyskinetic. The resting wall thickening was analyzed frame by frame in systole and % systolic wall thickening was obtained from 2-dimensional short axis images as follows:

$$100 \times (\text{end-systolic wall thickness} - \text{end-diastolic wall thickness}) / \text{end-diastolic wall thickness}.$$

The interpretation of the wall motion/thickening analysis

was performed by 2 experienced echocardiographers who were blind to the clinical data.

After the baseline echocardiographic examination, dobutamine was infused intravenously at a dose of $5 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$, with 0.5 mg of atropine if necessary, and increased by $5-10 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ every 3 min up to $40 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$. All echocardiographic images of the baseline and the DSE study were digitally obtained on-line and edited in quad screen cineloop format with simultaneous display of the rest, low-dose, peak dose, and recovery stages on optical disks. Those images were analyzed qualitatively using this quad screen cineloop format. The patterns of segmental response to dobutamine were defined according to a previous report.⁵

1. Biphasic: improvement of wall motion score ≥ 1 grade during the low-dose dobutamine study followed by deterioration during the high-dose dobutamine study.
2. Sustained improvement: improvement without deterioration of wall motion from low to peak dose of dobutamine.
3. Worsening: deterioration of wall motion during dobutamine infusion.
4. No change: absence of improvement or worsening during dobutamine infusion.

The myocardium was regarded as viable when segments showed any pattern other than the No. 4 pattern of the segmental response to dobutamine.

Reproducibility of the Data The interpretation of DSE was performed by 2 experienced observers who were blinded to the clinical data. The inter- and intraobserver variability of the results of analysis was 90% and 96% respectively.

Ultrasonic Integrated Backscatter

A commercially available 2-dimensional integrated backscatter imaging system (SONOS 2500, Hewlett-Packard, incorporating Acoustic Densitometry) was used to acquire and store IBS images of transthoracic parasternal long- and

Table 1 Clinical Differences Between Patients With a Left Ventricular Ejection Fraction <40% (Group A) and ≥40% (Group B)

	Group A (n=14)	Group B (n=16)	p value
Age (years)	64±11	65±10	NS
Gender (M/F)	10/4	11/5	NS
Vessel disease			
Single	1/14 (7%)	7/16 (44%)	<0.05
Double	7/14 (50%)	6/16 (37%)	NS
Triple	6/14 (43%)	3/16 (19%)	NS
Previous MI			
A	5/14 (36%)	9/16 (57%)	NS
IP	3/14 (21%)	6/16 (37%)	NS
A and IP	6/14 (43%)	1/16 (6%)	<0.05
LVEF before (%)	31±5*	51±6**	<0.01
LVEF after (%)	39±7	57±5	<0.01

Single, single vessel disease; Double, double vessel disease; Triple, triple vessel disease; MI, myocardial infarction; A, antero-septal infarction; IP, inferoposterior infarction; LVEF, left ventricular ejection fraction; before, before revascularization; after, after revascularization. *p<0.01 before and after revascularization in group A; **p<0.01 before and after revascularization in group B.

Table 2 Individual Responses to Dobutamine and Regional Function Recovery of Akinetic Segments

Segments	Site of MI		Recovery		DSE	
	Group A	Group B	Group A	Group B	Group A	Group B
1	A	A	+	+	-	-
2	IP	IP	+	-	+	-
3	IP	IP	+	+	+	+
4	IP	A	+	+	+	+
5	A	A	-	-	-	-
6	IP	A	+	+	+	+
7	A	A	-	+	-	+
8	A	IP	-	+	-	-
9	IP	A	+	+	+	+
10	A	A	+	-	+	-
11	IP	IP	+	+	+	+
12	IP	A	-	+	-	-
13	A	A	-	+	-	+
14	IP	IP	-	+	+	+
15	A	A	+	-	+	-
16	A	A	+	+	-	+
17	A	A	-	+	-	+
18	IP		-		-	
19	A		-		+	
20	IP		+		+	

MI, myocardial infarction; DSE, dobutamine stress echocardiography; A, antero-septal infarction; IP, inferoposterior infarction. DSE: (+) responsive to dobutamine by visual assessment; (-) nonresponsive to dobutamine by visual assessment. Recovery: (+) improved segment at follow-up study by visual assessment; (-) no change.

short-axis views in optical disks. The ultrasonic beam is always perpendicular to the target segments. This software allowed us to retrieve a continuous loop digital recording and to carry out off-line analysis of 2-dimensional backscatter images. We used a 31×31 pixel region of interest placed in the akinetic myocardium of the anterior septum, the inferoposterior wall, or both. The power of the integrated backscatter radiofrequency signal within the region of interest was measured in each frame (total 60 frames) and its decibels (dB) values were displayed in a table format. The value of IBS (y-axis) vs frames (x-axis) was displayed as the cardiac cycle-dependent variation curve of IBS at the same time. The operator controlled the location of the region of interest through the cardiac cycle and kept the image settings (transmission power, compression, time gain compensation, lateral gain control) for repeat follow-up studies with the same conditions. The magnitude of IBS-CV was calculated as the average in 3 consecutive cardiac cycles of the difference between the minimal and

maximal values of IBS (Fig 1A). The delay of IBS-CV was expressed as the time between the onset of the R wave and the nadir of IBS-CV divided by the QT interval^{16,17} When its delay is more than 1.2, IBS-CV is multiplied by -1 and called phase-corrected IBS-CV¹³ (Fig 1B).

Statistics

Statistical analysis was performed with SPSS version 10.0J for Windows (Chicago, IL, USA). Continuous variables were expressed as mean±1 SD. Student's t test for unpaired and paired data was used when appropriate. For the analysis of continuous data, Mann-Whitney rank sum tests were used. Groups were compared for categorical data using the chi-square test or Fisher's exact test. Sensitivity and specificity for predicting functional recovery were based on the standard definition. The temporal changes of some variables were analyzed with repeated-measure ANOVA. The optimal value of IBS to predict functional recovery was determined by receiver operating characteristic (ROC)

curve analysis. The optimal cutoff value was defined as that providing the highest sensitivity/specificity. A probability value less than 0.05 was considered significant for all tests.

Results

Study Population

Of the 48 patients studied, 30 were enrolled and divided into 2 groups according to LVEF (group A, $<40\%$, $n=14$; group B, $\geq 40\%$, $n=16$). The remaining 18 patients were excluded, 2 because of heart failure, 9 for restenosis and 7 for absence from the follow-up study. Baseline clinical characteristics are shown in Table 1. No significant differences were observed in age, gender, or the site of previous myocardial infarction between the 2 groups. There was a difference in the number of critically diseased vessels between groups A and B ($p<0.05$). In both groups, LVEF improved after PTCA (from 31 ± 5 to $39\pm 7\%$, from 51 ± 6 to

$57\pm 5\%$, $p<0.01$). There was a significant difference in LVEF between the 2 groups both before and after PTCA ($p<0.01$).

Systolic Wall Thickening and Functional Recovery

In group A, a total of 224 myocardial segments were analyzed, 20 of which demonstrated initially akinetic wall motion before PTCA, 10 in the anterior septum and 10 inferoposterior. Of those 20 segments, 11 (55%) showed improvement of wall motion on visual analysis after PTCA (Table 2). In group B, a total of 256 segments were analyzed, and 17 initially demonstrated akinetic wall motion before PTCA, 12 in the anterior septum and 5 inferoposterior. Of those 17 segments, 13 (76%) improved after PTCA on visual analysis (Table 2).

There was no difference in resting WT between segments that responded to dobutamine and those that did not in either group (group A, $10\pm 2\%$ vs $8\pm 4\%$; group B, $10\pm 1\%$ vs $9\pm 2\%$; $p=NS$). Resting WT improved significantly in the follow-up study (group A, from $9\pm 3\%$ to $18\pm 9\%$; group B, from $10\pm 2\%$ to $25\pm 10\%$; $p<0.01$). Although there was no difference in resting WT between group A and group B before PTCA, resting WT was significantly greater in group B than in group A ($18\pm 9\%$ vs $25\pm 10\%$, $p<0.05$) in the follow-up study (Fig 2). Among the segments showing improvement of wall motion in the follow-up study, there was no significant difference in resting WT between groups A and B (Fig 3). In the follow-up study, the improved segments showed a resting WT greater than 20%.

The optimal value of resting WT for predicting improvement of regional LV function was determined by ROC curve analysis. The cutoff value of 9.5 for resting WT yielded the highest sensitivity and specificity (Fig 4A). Using this cutoff value, resting WT had a sensitivity of 79% and a specificity of 54% as a whole, and there were no significant differences between group A and B in the diagnostic accuracy of resting WT (Table 3).

The measurements of resting WT were performed by 2 independent experienced observers. Interobserver and intraobserver variabilities for resting WT were $1\pm 0.6\%$ and $1\pm 0.4\%$ (the absolute difference) with no significant differences between observations.

Dobutamine Stress Echocardiography and Functional Recovery

All patients successfully underwent DSE studies. The mean dose of dobutamine at the peak stage was $30\pm 10\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$. End-points for this stage were chest pain in 11 patients and a biphasic pattern of segmental response to

Fig2. Changes of % systolic wall thickening. The % systolic wall thickening in group B improved much more than that of group A. Group A: patients with LVEF $<40\%$; Group B: patients with LVEF $\geq 40\%$. LVEF, left ventricular ejection fraction.

Fig3. Relationship between regional function recovery by visual analysis and % systolic wall thickening in a follow-up study.

Fig4. Receiver operating characteristic curve analysis showed a cutoff value of 9.5 for resting WT (A), 3.1 for the magnitude of resting IBS-CV (B), and 5.5 for that of DSE-IB (C), and yielded the highest sensitivity and specificity for predicting regional function recovery.

Table 3 Low-Dose DSE, Resting Wall Thickening, Resting IBS-CV, and DSE-IB for Prediction of Functional Recovery Using Respective Cutoff Values

Methods	No. of segments	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
<i>Low-dose DSE</i>					
Total	37	79 (19/24)	84 (11/13)	90 (19/21)	69 (11/16)
Group A	20	82 (9/11)	78 (7/ 9)	82 (9/11)	78 (7/ 9)
Group B	17	77 (10/13)	100 (4/ 4)	100 (10/10)	57 (4/ 7)
<i>Resting % wall thickening</i>					
Total	37	79 (19/24)	54 (7/13)	76 (19/25)	58 (7/12)
Group A	20	73 (8/11)	44 (4/ 9)	61 (8/13)	57 (4/ 7)
Group B	17	84 (11/13)	75 (3/ 4)	92 (11/12)	60 (3/ 5)
<i>Resting IBS-CV</i>					
Total	37	92 (23/25)	83 (10/12)	92 (23/25)	83 (10/12)
Group A	20	100 (12/12)	86 (7/ 8)	92 (12/13)	100 (7/ 7)
Group B	17	* 84 (11/13)	75 (3/ 4)	92 (11/12)	60 (3/ 5)
<i>DSE-IB</i>					
Total	37	** 62 (15/24)	69 (9/13)	79 (15/19)	50 (9/18)
Group A	20	54 (6/11)	67 (6/ 9)	67 (6/ 9)	54 (6/11)
Group B	17	69 (9/13)	75 (3/ 4)	90 (9/10)	43 (3/ 7)

DSE-IB, maximal magnitude of cyclic variation of integrated backscatter during dobutamine stress; Resting IBS-CV, maximal magnitude of cyclic variation of integrated backscatter at rest. *, ** $p < 0.05$. The numbers in the parentheses represent the segment numbers.

Table 4 Changes in Heart Rate, Mean Blood Pressure, and Rate-Pressure Product During Low-Dose Dobutamine Stress Echocardiography

	Group A		<i>p</i> (group A vs group B)	Group B	
	Control	10 $\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ of dobutamine		Control	10 $\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ of dobutamine
HR (beats/min)	70 $\pm$ 12	86 $\pm$ 15*	NS	63 $\pm$ 8	77 $\pm$ 16*
Mean BP (mmHg)	87 $\pm$ 12	96 $\pm$ 14*	NS	95 $\pm$ 9	104 $\pm$ 17
RPP (mmHg $\cdot$ beats/min)	8,194 $\pm$ 2,079	11,780 $\pm$ 3,010*	NS	8,272 $\pm$ 1,924	11,527 $\pm$ 2,809*

HR, heart rate; BP, blood pressure; RPP, rate-pressure product. * $p < 0.01$ control and dobutamine stress in each group.

dobutamine in 19 patients. None of the 30 patients had significant side effects. The data of low-dose DSE was used to analyze LV functional recovery. Heart rate, mean blood pressure, and the rate-pressure product increased significantly at a dose of 10 $\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ of dobutamine in both groups A and B. There was no significant difference in these parameters between the 2 groups (Table 4).

Nineteen of the 37 segments initially demonstrating akinetic wall motion before PTCA responded to low doses of dobutamine, whereas 11 segments did not. Overall, low-dose DSE had a sensitivity of 79%, a specificity of 84%, a positive predictive value of 90%, and a negative predictive value of 69% in predicting improvement of regional LV function (Table 3). In group A, its specificity was relatively low (78%) and in group B, its sensitivity was relatively low (77%). There were no significant differences between group A and B in the diagnostic accuracy of low-dose DSE (Table 3).

Cardiac Cycle-Dependent Variation of Ultrasonic Integrated Backscatter and Functional Recovery

The magnitude and the degree of asynchrony of IBS-CV were measured in the anterior septum and the inferoposterior wall from the short-axis views of the left ventricle. The magnitude of phase-corrected IBS-CV was similar in patients with previous (≥ 9 months after the onset) myocardial infarction and those with previous (< 9 months) myocardial infarction (2.1 $\pm$ 3.5 and 2.4 $\pm$ 3.0 dB, respectively, $p = \text{NS}$). The average magnitude of phase-corrected IBS-CV showed no difference between the 2 groups in the control, follow-up, and DSE studies in group A (Fig 5A). In group

Fig 5. Individual values of phase-corrected magnitude of cyclic variation of integrated backscatter (IBS-CV) in control, follow-up, and dobutamine stress echocardiographic studies. Open circles = group A; triangles = group B. Group A: patients with LVEF $< 40\%$; Group B: patients with LVEF $\geq 40\%$. LVEF, left ventricular ejection fraction.

B, phase-corrected IBS-CV in the follow-up study was significantly higher than that in the control ($p < 0.05$) (Fig 5B). The time delay of IBS-CV was similar in both groups (1.1 $\pm$ 0.1 vs 1.0 $\pm$ 0.1, $p = \text{NS}$). The optimal value of resting IBS-CV and DSE-IB for predicting improvement of regional LV function was determined by ROC curve analysis. The ROC curve analysis demonstrated that the cutoff value of 3.1 for the magnitude of resting IBS-CV (Fig 4B)

and of 5.5 for the magnitude of DSE-IB (Fig 4C) yielded the highest sensitivity and specificity. Using these cutoff values, resting IBS-CV had a sensitivity of 92%, a specificity of 83%, a positive predictive value of 92%, and a negative predictive value of 83%. In group B, however, resting IBS-CV had a sensitivity of 84% and a specificity of 75%. DSE-IB showed a sensitivity of 62% ($p < 0.05$ vs IBS-CV), a specificity of 69%, a positive predictive value of 79%, and a negative predictive value of 50% (Table 3). In group A, DSE-IB showed a sensitivity of 54% ($p < 0.05$ vs IBS-CV). There were no significant differences between group A and B in the diagnostic accuracies of resting IBS-CV and DSE-IB (Table 3).

The measurements of IBS-CV and DSE-IB were performed by 2 independent experienced observers. Interobserver and intraobserver variabilities for the magnitude of IBS-CV were 0.7 ± 0.5 dB and 0.8 ± 0.6 dB (the absolute difference) with no significant difference between observations; for the magnitude of DSE-IB, interobserver and intraobserver variabilities were 0.8 ± 0.7 and 0.8 ± 0.6 dB (the absolute difference) with no significant difference between observations.

Discussion

The main findings of our study were that (1) low-dose DSE has a high sensitivity/specificity for prediction of LV functional recovery in patients with chronic LV ischemic dysfunction, consistent with previous studies, (2) not only DSE at a low dose, but also resting IBS-CV is a useful predictor for functional recovery after revascularization, (3) particularly in patients with a LVEF $< 40\%$, resting IBS-CV may be an excellent predictor of functional recovery, and (4) the global LV function may not affect the diagnostic accuracies of resting WT, low-dose DSE, resting IBS-CV and DSE-IB.

Effect of Reperfusion on IBS-CV

In the setting of acute myocardial ischemia, or acute myocardial infarction, IBS-CV is blunted initially and its magnitude is increased after revascularization. The improvement of IBS-CV depends on the severity of ischemic injury and reflects the maintenance of regional intramural contractile function^{13,18}

In the setting of chronic LV ischemic dysfunction, resting IBS-CV correlates with the contractile reserve.¹⁴ However, the efficacy of resting IBS-CV in predicting functional recovery after revascularization in patients with chronic LV ischemic dysfunction still remains unknown.

Chronic Left Ventricular Ischemic Dysfunction and Integrated Backscatter Cyclic Variation

Chronic hypoperfusion in patients with myocardial infarction may result in reduction of myocardial blood flow¹⁹ and progressive ultrastructural alterations, depletion of the contractile apparatus, deposition of glycogen, loss of sarcoplasmic reticulum, and loss of sarcomeres from the cells.²⁰⁻²⁶ The time course and degree of functional recovery after successful revascularization depends on the severity of structural damage in the regional myocardium including the myocyte and nonmyocyte compartments.²⁴⁻²⁷ Previous study has shown that chronically hypoperfused myocardium or even well perfused myocardium detected by scintigraphy may not recover after successful revascularization.^{6,7,26} This means that evaluation of the status of the contractile appa-

ratus as well as of myocardial perfusion is important in predicting functional recovery.

In experimental studies, IBS-CV was independent of blood flow and varied systematically with the contractile state in both bullfrog gastrocnemius and canine myocardium even if they differed in the directional change of IBS-CV.^{9,10,28} Wickline et al reported that sarcomere shortening would affect intracellular acoustic impedance, which determines IBS-CV, and that the myocardial contractile reserve is mainly contributed by the outer wall fibers.¹² This is the reason why IBS-CV can be an appropriate tool for evaluating whether or not a primarily akinetic segment will recover after revascularization.

Pasquet et al surmised in their clinical study of patients with chronic LV ischemic dysfunction caused by subendocardial damage, an excessive afterload, or both that initially dysfunctional segments exhibiting IBS-CV contract isometrically. The IBS-CV is independent of resting wall motion or thickening, and that correlates with contractile reserve when using dobutamine infusion.¹⁴ In the present study, the value of resting IBS-CV could not be compared with dobutamine stress WT (inotropic reserve) because image quality was inadequate to allow evaluation. However, most of the segments in which the resting IBS-CV was more than 3.1 responded to dobutamine. Ten segments showed a temporal delay in resting IBS-CV in this study, and 6 out of 10 segments recovered their function. In both groups A and B, the segments with an absolute value of resting IBS-CV greater than 3.1 regained their function. The mechanism of delayed IBS-CV may have been asynchronous contraction or delayed relaxation^{29,30} and stretching or passing distention¹¹ in the ischemic myocardium.

Prediction of Functional Recovery in Chronic Left Ventricular Ischemic Dysfunction

Although resting IBS-CV and DSE were sensitive in predicting functional recovery after revascularization, DSE-IB was less sensitive than either technique (92% for resting IBS-CV, 79% for DSE and 62% for DSE-IB). The reason for this may have been that DSE-IB in the infarcted segments did not correlate with the % systolic wall thickening during dobutamine infusion and that there were anisotropic effects of integrated backscatter or tethering effects in some cases during dobutamine stress.³¹ From clinical experience, the diagnostic accuracies of resting WT and DSE-IB are relatively low (unpublished data).

In the present study, ROC curve analysis was performed to determine the appropriate cutoff value of IBS-CV for prediction of functional recovery. Using a cutoff value of 3.1 on resting IBS-CV, a sensitivity of 92% and a specificity of 83% were obtained. In patients with a LVEF $< 40\%$ in particular, resting IBS-CV was an excellent predictor of functional recovery as well as DSE (100% and 86% for resting IBS-CV, 82% and 78% for DSE). The lower specificity for DSE could be attributed to the following possibilities: (1) tethering effects of the adjacent segments, (2) subendocardial scarring with a viable epicardial layer, and (3) excessive afterload. The sensitivity of DSE in patients with LVEF $\geq 40\%$ was low and may have been because the improvement of wall motion can be quite subtle. On the other hand, resting IBS-CV had a lower specificity in patients with LVEF $\geq 40\%$, possibly because of severe damage or scarring of the subendocardial muscle that prevented functional recovery despite revascularization. We could not assess resting IBS-CV of the subendo-

cardium and the epicardium separately. However, the present findings demonstrate that resting IBS-CV may be a suitable tool for predicting regional function recovery of initially akinetic segments in patients with LVEF<40%. Bax et al reported that in patients with chronic LV ischemic dysfunction (mean LVEF=27%), those with ≥ 4 viable segments assessed by DSE showed more improvement in symptoms and better prognosis than those with patients with <4 viable segments.³² In this regard, resting IBS-CV may be an adjuvant predictor of LV functional recovery.

The findings of the present study did not lend support to our hypothesis that the global LV function affects the diagnostic accuracies of DSE and IBS-CV in the prediction of regional function recovery. One reason for this may be that not only the global LV function affects those diagnostic accuracies. Furthermore, the small sample of patients may prevent the establishment of conclusions. Further investigation is needed to evaluate the usefulness of resting IBS-CV in a large number of patients.

Study Limitations

(1) The number of patients included in this study is so small that we could not evaluate the relation between the segments with delayed IBS-CV, which responded to dobutamine, and their functional recovery. (2) It was also difficult to differentiate between endocardium and epicardium in infarcted myocardium, so we could not evaluate resting IBS-CV of both layers separately. (3) The ultrasonic beam should be perpendicular to the myocardium in the IBS study, but we could not confirm this during DSE. (4) We could not assess all LV segments because of the characteristics of IBS.

Conclusions

The present study demonstrated that both resting IBS-CV and DSE are useful predictors for regional function recovery in patients with chronic LV ischemic dysfunction and that resting IBS-CV in particular had an excellent potential in patients with LVEF<40%. The usefulness of resting IBS-CV as an ancillary tool to DSE in cases of severely reduced LV function needs to be investigated in further studies

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