Role of Exercise Echocardiography as a Predictor of Coronary Artery Disease

Detection of Exercise-Induced Asynergy by M-Mode Echocardiography

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SUMMARY

Left ventricular asynergy has been shown to occur commonly in patients with coronary artery disease (CAD) and to be induced or exaggerated by exercise. The purpose of this study is to report on a method to detect asynergy and estimate its severity by M-mode echocardiographic analysis of left ventricular wall motion at rest and during supine ergometric exercise. Sixteen patients with CAD underwent graded supine ergometric exercise until anginal pain occurred or apparent ischemic changes were noted on ECG.

This study was done using the following criteria:

1) Asynergy at rest was defined as occurring when the amplitudes of the interventricular septum and/or the posterior left ventricular wall were below normal values at rest.

2) Asynergy during exercise was defined as occurring when one or both of the two amplitudes were more than 2 mm below the values at rest (severe) or were unchanged in spite of sufficient exercise load (mild).

The results were as follows:

1) In the normal subjects, the septal and posterior wall amplitudes increased during exercise (ranging from 7 mm to 9 mm for the septum, and from 13 mm to 16 mm for the posterior wall). In patients with CAD, asynergy at rest was demonstrated in only 3 cases (19%), whereas septal and/or posterior wall asynergy during exercise was noted in 75% of cases.

2) The location of exercise-induced asynergy detected by echocardiography showed a good correlation with that of coronary artery lesions ($\geq 75\%$ stenosis) recognized by angiography.

3) Significant differences were observed between changes in

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left ventricular dimensions in patients with CAD and those of normals during exercise. In the normal subjects, left ventricular end-systolic dimension (ESD) decreased without significant change in end-diastolic dimension (EDD) during exercise. On the other hand, both ESD and EDD increased during exercise in patients with CAD. Although echocardiographic analysis of left ventricular wall motion during exercise has some limitations, this study suggests that asynergy induced or exaggerated by ergometric exercise can be successfully detected by M-mode echocardiography.

Additional Indexing Words:

Ergometric exercise Left ventricular dimensions Frank-Starling effect

ABNORMALITIES in left ventricular wall motion (asynergy) have been shown to occur commonly in patients with coronary artery disease (CAD).¹⁾ It is widely accepted that asynergy is one of the most important factors which may worsen left ventricular global function in patients with CAD.^{2),3)} It is well known that some patients with severely stenosed coronary arteries have normal left ventricular wall motion at rest. Recent studies, however, have reported that asynergy is induced or exaggerated by exercise.⁴⁾⁻⁷⁾ Therefore, it is clinically important to examine left ventricular wall motion during exercise. Although echocardiography has proved useful in detecting left ventricular asynergy at rest,⁸⁾⁻¹²⁾ more accurate estimation of left ventricular function in patients with CAD requires echocardiographic analysis of LV wall motion during exercise to detect exercise-induced asynergy. The purpose of this study is to report on a method to detect and estimate asynergy by M-mode echocardiographic analysis of left ventricular wall motion at rest and during supine ergometric exercise.

METHOD AND MATERIALS

Study population (Table I)

Sixteen patients with CAD (2 females and 14 males) and 21 normal subjects (3 females and 18 males) were examined in this study. The average age of patients was 50 years with a range from 31 to 62 years. All patients had coronary artery disease confirmed by coronary angiography (luminal narrowing $\geq 75\%$ in at least one coronary artery). Exercise tests were performed within 1 week before coronary cineangiography. In no patient did persistent arrhythmias occur either at rest or during exercise. Seven patients with old myocardial infarction (more than 6 months before this study) were included. The average age of normal subjects was 29 years with a

Table I. Study Population

Patient No.	Sex	Age	Diagnosis	Exercise data*			ECG leads positive	EF (%)	No. vessels narrowed	Angiographic data			
				Resting HR	Maximum HR	HR for echo				LM	LAD	LCX	RCA
1	M	56	OMI	90	107	107	I, II, III, F, V ₃₋₆	55	3	0	75	100	90
2	M	47	ANG	80	100	100	II, III, F, V ₅₋₆	53	1	0	50	90	0
3	M	60	ANG	61	90	90	I, II, F	44	1	0	0	0	100
4	M	51	ANG	60	95	95	II, III, F, V ₃₋₆	70	1	0	0	100	0
5	M	59	ANG	67	102	102	II, III, F, V ₃₋₆	56	1	50	25	90	0
6	M	47	OMI	68	105	105	II, III, F	66	1	0	0	0	90
7	M	31	OMI	58	110	110	II, III, F	75	1	0	0	0	100
8	M	52	OMI	80	118	118	I, II, III, F, V ₃₋₆	41	2	0	90	100	25
9	M	51	ANG	55	100	100	V ₃₋₆	62	1	0	100	25	25
10	M	54	ANG	52	80	80	II, III, F, V ₅₋₆	71	1	0	99	0	0
11	M	42	ANG	65	120	120	I, V ₅₋₆	73	2	0	75	75	0
12	M	49	ANG	65	88	88	V ₅₋₆	83	1	0	75	0	0
13	F	42	ANG	70	135	135	II, III, F, V ₅₋₆	78	1	0	75	0	0
14	F	62	OMI	77	109	109	II, III, F, V ₄₋₆	37	3	0	90	100	99
15	M	50	OMI	76	133	133	V ₄₋₆	39	1	0	0	0	100
16	M	49	OMI	55	90	90	II, III, F, V ₄₋₆	53	1	0	100	25	25
Normals (n=21)				69±10	132±13	105±16	None						

Abbreviations: EF=ejection fraction; HR=heart rate; LAD=left anterior descending artery; LCX=left circumflex artery; LM=left coronary main trunk; RCA=right coronary artery; OMI=old myocardial infarction; ANG=angina pectoris.
* ECG positive: Downsloping ST segment depression of at least 0.1 mV.

range from 16 to 54 years and none had physical, electrocardiographic or echocardiographic abnormalities.

Exercise echocardiography

Patients and normal subjects exercised in the supine position using a Godart Lanooy ergometer. Graded exercise (a work load of 0.8 Watt/Kg for the first 3 min increasing by 10 Watts every 3 min) was performed until typical anginal pain occurred and/or apparent ischemic ECG changes were noted. Exercise was stopped due to the occurrence of anginal pain with ischemic ECG changes in 12 patients. On the other hand, the end point of exercise was the appearance of ischemic ECG changes without anginal pain in 4 patients. Ischemic ECG changes were defined as a horizontal or down-sloping ST depression (≥ 0.1 mV). The normal subjects exercised for at least 9 min until leg fatigue occurred. Twelve-lead electrocardiograms and M-mode echocardiograms were recorded at rest, every minute during exercise, and every 6 min after exercise using an Aloka SSD-110 ultrasonoscope and a 2.25 MHz internally focused transducer interfaced to a Honeywell model 1856 strip chart recorder set at a paper speed of 50 mm/sec. Echocardiography was performed in the standard manner. At higher exercise levels, it was very difficult to record good-quality echograms mainly due to bodily movements and tachycardia. Therefore, echocardiographic analysis during exercise in the normal subjects was done during the last 1 min of the third exercise level.

Echocardiographic analysis of LV wall motion abnormalities

Asynergy was defined by the following criteria:

- 1) Asynergy at rest was defined as the occurrence of septal and/or posterior wall amplitudes below normal values in normal subjects at rest (septal and posterior wall amplitudes ranged from 3 mm to 8 mm and 9 mm to 15 mm, respectively).

- 2) Asynergy during exercise was defined as occurring when one or both of the two amplitudes were more than 2 mm below the values at rest (severe) or were unchanged in spite of sufficient exercise load (mild). It was possible that left ventricular wall motion was unchanged during exercise due to insufficient exercise load. On the other hand, unchanged left ventricular wall amplitudes might be interpreted as being indicative of mild asynergy when the heart rate at the time of echocardiographic recordings during exercise was over 100/min, that is, when exercise load was sufficient. Echocardiographic analysis was done using the recordings obtained during expiration in order to minimize respiratory variation. Statistical evaluation was carried out by paired t test.

RESULTS

Analysis of LV wall motion at rest and during exercise by echocardiography

In the normal subjects, the septal amplitude increased significantly from 7.1 ± 0.3 mm (mean $\pm$ SEM) at rest to 9.0 ± 0.4 mm during exercise ($p < 0.001$). Furthermore, the posterior wall amplitude increased significantly from 13.2 ± 0.4 mm at rest to 15.8 ± 0.5 mm during exercise ($p < 0.001$). However, there were some subjects in whom the septal or posterior wall amplitude was unchanged during exercise. That is, the septal and posterior wall amplitudes were unchanged during exercise in 5 (24%) and 6 (29%) subjects, respectively. Fig. 1 shows echograms at rest and during exercise in a normal subject. Both the septal and posterior wall amplitudes increased markedly in this subject.

In patients with CAD, abnormalities in posterior wall motion at rest were seen in 3 patients (Cases 1, 2, 14). Posterior wall asynergy at rest was not noted in the other 8 patients with stenotic lesions of the left circumflex artery (LCX) and/or right coronary artery (RCA). Although there were 2 cases with complete obstruction of the left anterior descending artery (LAD),

Fig. 1. Echocardiograms at rest (upper) and during exercise (lower) in a normal subject. Both the septal and posterior wall amplitudes increased during exercise.

Fig. 2. Echocardiograms at rest (upper) and during exercise (lower) in a patient with coronary artery disease. The posterior wall amplitude decreased remarkably, while the septal amplitude increased during exercise in this patient.

septal asynergy at rest was not detected echocardiographically in these patients. The obstruction of the LAD in these 2 cases (Cases 9, 16) was distal to the origin of the first septal branch. Of the 16 patients with CAD, severe asynergy of the septum and the posterior wall during exercise was seen in 4 (25%) and 6 (38%) cases, respectively. For example, a decrease in posterior wall amplitude was observed with a compensatory increase in septal amplitude in a patient with an old posterior wall infarction (Fig. 2). Another example is shown in Fig. 3. In this patient, a decrease in septal amplitude with a compensatory increase in posterior wall amplitude was revealed echocardiographically. On the other hand, mild asynergy of the septum and posterior wall was detected in 3 (19%) and 2 (13%) patients, respectively. An example of mild asynergy is shown in Fig. 4. This patient had significant stenotic lesions in both the LAD and LCX. Septal and posterior wall amplitudes at rest were within normal limits. Although the heart rate increased from 65 at rest to 120 during exercise and significant ST depression was observed, both amplitudes were unchanged. As shown in Table II, asynergy at rest was demonstrated in only 3 (19%) cases, whereas exercise-induced asynergy was noted in 12 (75%) cases (Table II). Of 12 patients in whom

Fig. 3. Another example of echograms in a patient with coronary artery disease. In this patient, decrease in the septal amplitude with a compensatory increase in the posterior wall amplitude was observed echocardiographically.

Fig. 4. Echocardiograms in which mild asynergy was observed. In this patient, LV wall motion was normal at rest. Both amplitudes were unchanged during exercise in spite of sufficient exercise load.

Table II. Frequency with Which Left Ventricular Asynergy Was Observed at Rest and during Exercise

Asynergy at rest	During exercise		
	severe asynergy	mild asynergy	total
3/16 (19%)	9/16 (56%)	3/16 (19%)	12/16 (75%)

the end point of exercise was the occurrence of anginal pain, severe asynergy was detected in 7 cases. Of 4 patients in whom exercise was stopped due to the appearance of ischemic ECG changes without anginal pain, severe asynergy was induced in 2 cases.

Correlation between the locations of exercise-induced asynergy on echocardiography and those of stenotic lesions on coronary angiography

Of 9 cases with stenotic lesions of the LAD, severe and mild asynergy of the septum was seen in 4 (44%) and 2 (22%) cases, respectively (Table III). Although mild septal asynergy was seen in 1 (14%) of 7 patients without LAD lesions, severe asynergy was not detected in these patients (Table III). Of 11 cases with stenotic lesions of the LCX and/or RCA, severe and mild asynergy of the posterior wall was revealed in 6 (55%) and 2 (18%) cases, respectively (Table III). Of 5 cases without LCX and RCA lesions, neither severe nor mild asynergy was detected (Table III). Severe or mild asynergy of the septum was found in 6 of 9 cases with LAD lesions, giving a sensitivity of 67%. Normal septal wall motion was seen in 6 of 7 cases without LAD lesions, for a specificity of 86%. Severe or mild asynergy of the posterior wall was found in 8 out of 11 cases with LCX and/or RCA lesions, for a sensitivity of 73%. Normal posterior wall motion was found in 5 out of 5 cases with neither LCX nor RCA lesions, for a specificity of 100%. Of 9 cases with

Table III. The Relationship between the Location of Stenotic Coronary Artery Lesions and That of Exercise-Induced Asynergy

	No.	Asynergy of the septum		
		severe	mild	total
Stenotic lesions (+) in LAD	9	4	2	6 (67%)
Stenotic lesions (-) in LAD	7	0	1	1 (14%)
	No.	Asynergy of the posterior wall		
		severe	mild	total
Stenotic lesions (+) in LCX and/or RCA	11	6	3	8 (73%)
Stenotic lesions (-) in both LCX and RCA	5	0	0	0 (0%)

LAD=left anterior descending artery; LCX=left circumflex artery; RCA=right coronary artery.

Table IV. Comparison of Proximal Lesions with Distal Lesions and Influence of Dominancy of Coronary Circulation to LV Posterior Wall

The location of stenotic lesions	No.	Asynergy of the septum			
		Rest	Exercise		
			severe	mild	total
proximal LAD	3	0	2	1	3 (100%)
distal LAD	6	0	2	1	3 (50%)

The location of stenotic lesions	No.	Asynergy of the posterior wall			
		Rest	Exercise		
			severe	mild	total
proximal LCX and/or RCA	7	2	4	1	5 (71%)
only distal	4	1	2	1	3 (75%)
dominant vessel or balanced type	8	3	5	2	7 (88%)
only non-dominant vessel	3	0	1	0	1 (33%)

LAD=left anterior descending artery; LCX=left circumflex artery; RCA=right coronary artery.

stenotic lesions of the LAD, there were 3 cases with proximal lesions (proximal to the origin of the first septal branch) and 6 cases with distal lesions (distal to the origin of the first septal branch). Severe or mild asynergy was seen in all 3 cases (100%) with proximal lesions. On the other hand, severe or mild asynergy was seen in 3 (50%) of 6 cases with distal lesions (Table IV). Of 11 cases with stenotic lesions of the LCX and/or RCA, there were 7 cases with proximal lesions (LCX: proximal to the origin of the obtuse marginal branch; RCA: proximal to the origin of the anterior right ventricular branch) and 4 cases with only distal lesions. Of 7 case with proximal lesions of either the LCX or RCA, severe or mild asynergy was seen in 5 cases (71%). On the other hand, severe or mild asynergy was seen in 3 (75%) of 4 cases with only distal lesions. Of 8 cases whose stenotic lesions existed in the vessel which perfused the left ventricular posterior wall dominantly or at least equally, severe or mild asynergy was detected in 7 cases (88%) (Table IV). Of 3 cases whose stenotic lesions existed in only the non-dominant vessel, exercise-induced asynergy was seen in only 1 case (33%) (Table IV).

Left ventricular dimensions at rest and during exercise

Obvious differences were observed between LV dimensions (end-systolic dimension: ESD; end-diastolic dimension: EDD) in patients with CAD and the normals (Fig. 5). Normal subjects manifested a significant decrease ($p<0.001$) in mean ESD (28.9 ± 0.3 mm to 25.3 ± 0.8 mm), whereas a significant increase ($p<0.001$) in mean ESD was seen in patients with CAD (34.7

Fig. 5. Left ventricular dimensions at rest and during exercise. In the normals, ESD was significantly decreased, while EDD remained unchanged during exercise. On the other hand, both ESD and EDD significantly increased during exercise in patients with CAD. The values represent mean $\pm$ SEM. CAD=coronary artery disease; E=exercise; EDD=end-diastolic dimension; ESD=end-systolic dimension; R=rest.

± 1.6 mm to 37.6 ± 2.0 mm). EDD significantly increased during exercise (50.9 ± 2.0 mm vs 55.1 ± 1.8 mm) in patients with CAD ($p < 0.001$). On the other hand, there was no significant change in mean EDD (47.2 ± 0.6 mm vs 48.0 ± 0.7 mm) in the normals.

DISCUSSION

Regional left ventricular wall motion abnormalities (asynergy) have been shown to occur commonly in patients with CAD.¹⁾ Since Herman et al^{2),3)} reported that LV global function might be worsened by asynergy, many investigations concerning the correlation between asynergy and LV function have been reported.¹³⁾⁻¹⁸⁾ LV asynergy has been examined mainly by invasive methods such as contrast ventriculography.¹³⁾⁻¹⁸⁾ Recently, Feigenbaum et al¹⁰⁾⁻¹²⁾ reported that echocardiography was a useful non-invasive method for the estimation of asynergy. It is well known that there are some cases with significant stenosis of one or more coronary arteries who have no abnormal wall motion at rest. In these patients with normal LV wall motion at rest, however, it has been frequently observed that LV asynergy is often induced or exaggerated by atrial pacing or exercise.⁴⁾⁻⁷⁾ Fogelman et al¹⁹⁾ reported a remarkable decrease in LV posterior wall diastolic endocardial velocity when anginal pain was induced by exercise in patients with angina pectoris. Mason et al²⁰⁾ reported that in patients with CAD, exercise echocardiography was a sensitive method of detecting wall motion abnor-

malities secondary to exercise-induced ischemia by analysis of regional wall thickening and thinning.

Technical problems in exercise echocardiography

Mason et al²⁰⁾ mentioned that amplitudes were not appropriate indices in exercise echocardiography because they were apt to be influenced by artifacts. In order to minimize the influence of respiration, only echograms obtained during expiration were analyzed both at rest and during exercise. Moreover, in order to minimize the influence of the patient's bodily movements during exercise, their shoulders were fixed to the bed. We attempted to exclude exercise induced artifacts in this manner. In spite of these careful procedures, the difficulty in recording high-quality echograms was the greatest limitation of this method, as Mason²⁰⁾ mentioned. For instance, we could not record good echograms both at rest and during exercise in patients with pulmonary emphysema and/or obesity. Therefore those patients in whom good-quality echograms could not be recorded were excluded from this study.

Analysis of LV wall motion at rest and during exercise by echocardiography

Although there were 7 cases with old myocardial infarctions and 8 cases with complete obstruction of at least one coronary artery included in this study, left ventricular asynergy at rest was detected echocardiographically in only a few cases. The reasons why left ventricular asynergy at rest was seen in so few cases were as follows: first, the extent of the left ventricular wall which can be detected by M-mode echocardiography is limited and it is very difficult to obtain good-quality echograms of the anterolateral and apical regions where wall motion abnormalities are likely to occur in patients with CAD. That is, left ventricular wall motion abnormalities cannot be detected in cases with distal or peripheral lesions of the coronary arteries, even though the lesions are completely obstructive. The second, and most important reason, is that those cases with apparent akinetic or severely hypokinetic motion at rest were excluded from the study because the purpose of this study was to detect exercise-induced asynergy. Asynergy during exercise was defined as occurring when one or both of the two amplitudes was more than 2 mm below the values at rest (severe) or unchanged in spite of sufficient exercise load (mild). Severe asynergy of the septum and the posterior wall was seen in only 25% and 38% of cases, respectively.

However, there were many cases in whom the septal and/or posterior wall amplitudes were unchanged during exercise. Even in some normal subjects, the septal and/or posterior wall amplitudes did not increase significantly during exercise probably due to insufficient exercise load. However, there were some cases in whom both the septal and posterior wall amplitudes were unchanged during exercise in spite of a sufficient increase of heart rate

and appearance of significant ST depression on the ECG such as was shown in Fig. 5. Therefore, cases where the left ventricular wall amplitudes were unchanged in spite of sufficient exercise load were regarded as exhibiting mild asynergy. Using these criteria, severe or mild asynergy of the septum and posterior wall during exercise was seen in 75% of cases.

Correlation between the location of exercise-induced asynergy demonstrated by echocardiography and that of stenotic lesions seen on coronary angiography

The location of exercise-induced asynergy demonstrated by echocardiography showed good correlation with that of stenotic lesions seen on coronary angiography. That is, septal asynergy during exercise was detected in 67% of patients with LAD lesions and posterior wall asynergy during exercise was detected in 73% of patients with LCX and/or RCA lesions. Thus, the specificity of exercise echocardiography was very high. As is the case in patients at rest, the extent of the LV wall which can be detected by M-mode echocardiography during exercise is limited. Furthermore, exercise-induced asynergy may not be observed in cases with distal or peripheral lesions of the LAD, although it may be noted in cases with proximal lesions.^{21), 22)} However, in our study exercise-induced asynergy was detected with a high frequency in those cases with only distal lesions of the LCX and/or RCA as well as those with proximal lesions. The reason why exercise-induced asynergy was noted in those cases with only distal lesions might have been that the stenotic lesions were multiple. Development of collateral circulation associated with the stenotic lesions also might influence the regional wall motion. It was thought that one of the advantages of exercise echocardiography was that exercise-induced asynergy could be detected in almost all patients with proximal lesions which might influence global LV function. Perfusion characteristics of the LV posterior wall were classified into 3 types, that is, LCX dominant, RCA dominant, and a balanced type. Exercise-induced asynergy in patients with stenotic lesions in dominant vessels and with stenotic lesions only in non-dominant vessels was detected in 88% and 33% of cases, respectively. Therefore, it was thought that the dominance of coronary perfusion influenced the occurrence of exercise-induced asynergy in the LV posterior wall.

Left ventricular dimensions at rest and during exercise

In normal subjects, ESD was significantly decreased with unchanged EDD during exercise. This suggests that the principal cardiovascular response of normals to exercise is not only increased heart rate, but also enhanced cardiac contractility.^{23), 24)} More recently, Weiss et al²⁵⁾ reported that the Frank-Starling effect appeared to be reserved in normal subjects for augmenting cardiac performance during severe semisupine exertion. However, the Frank-Starling mechanism played a minor role during exercise in the

normal subjects of this study, because their EDD did not increase significantly. It is well known that measurements of left ventricular end-systolic volume obtained from echocardiographic measurements are unreliable in patients with CAD. However, echocardiography can provide reliable measurements of left ventricular end-diastolic volume (EDV) in patients with CAD.²⁶⁾ Therefore, EDD is thought to be one of the relatively reliable indices of EDV. In patients with CAD, EDD increased significantly during exercise. This suggests that compensation by the Frank-Starling mechanism may be activated by exercise in patients with CAD, because cardiac contractility might be impaired by exercise-induced asynergy.^{27),28)}

Clinical implications

Though there are some limitations in the evaluation of left ventricular regional wall motion by exercise echocardiography, this method is simple, easily repeatable, and has high specificity for coronary artery lesions. Moreover, because it is possible to observe the dimensional changes of the left ventricle with this technique, exercise echocardiography is one of the useful methods of assessing left ventricular global function.

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