HEMODYNAMIC PARAMETERS DURING DYNAMIC EXERCISE IN PATIENTS WITH SILENT MYOCARDIAL ISCHEMIA IN THE PRESENCE OR ABSENCE OF HYPERTROPHY

JUNSHI YOSHIDA, M.D., MITSUHIRO YOKOTA, M.D. Ph.D.*
TAKASHI MIYAHARA, M.D. Ph.D., KEIKO MATSUBARA, M.D.
TOSHIKAZU SOBUE, M.D. AND HIDEHIKO SAITO, M.D. Ph.D.

Hemodynamic parameters during supine leg exercise-induced myocardial ischemia were investigated in ten patients without left ventricular hypertrophy (group I), and in ten patients with left ventricular hypertrophy (group II). Both groups of patients had previously been diagnosed as having totally asymptomatic silent myocardial ischemia. Both groups were comparable in age, sex, left ventricular ejection fraction at rest, and extent of coronary artery disease. All of the patients exercised to the same extent without angina or its usual equivalent. Left ventricular filling pressure increased from 4 ± 2 mmHg at rest to 11 ± 3 mmHg at peak exercise in group I, and from 7 ± 4 mmHg at rest to 19 ± 7 mmHg at peak exercise in group II. Left ventricular filling pressure at peak exercise was significantly greater in group II than in group I ($p < 0.01$). Totally asymptomatic silent myocardial ischemia can be seen with either normal or mildly abnormal left ventricular filling dynamics during exercise. In addition, patients with coexistent left ventricular hypertrophy can have severely abnormal left ventricular filling dynamics during exercise without ischemic cardiac pains. Therefore, severe ischemia and/or stretching of the ventricular wall may be necessary, but not sufficient, for the occurrence of chest pain.

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ANGINA pectoris has been the classic marker used to identify patients with significant fixed atherosclerotic coronary artery disease and/or alterations in dynamic coronary artery tone in the presence of narrowing (usually due to atherosclerosis). However, an increasing number of studies support the concept that many patients with coronary artery disease have transient myocardial

ischemia which is clinically “silent” during daily activities^{1–6}. When these patients undergo exercise stress testing, asymptomatic ST-segment depression is a common finding^{6–8}. Among patients with chronic stable angina who exhibit ST-segment depression during exercise, ambulatory electrocardiographic (ECG) monitoring during daily activities can be used to identify transient ischemic episodes in approximately 40–50% of patients⁹. The exercise stress test is still the established procedure for assessing myocardial ischemic responses in persons with

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*Department of Clinical Laboratory Medicine, Nagoya University Hospital; and First Department of Internal Medicine, Nagoya University School of Medicine, Nagoya, Japan

Mailing address: Mitsuhiro Yokota, M.D., PhD Associate Professor of Medicine Department of Clinical Laboratory Medicine Nagoya University School of Medicine, 65 Tsurumai-cho, Showa-ku, Nagoya 466, Japan

known or suspected coronary artery disease.

It has been shown that left ventricular filling pressure often increases dramatically during an attack of angina pectoris.¹⁰⁻¹⁷ Many studies have shown that this increase in filling pressure reflects both reduced left ventricular distensibility and systolic dysfunction, with the diastolic abnormality usually predominant. Furthermore, a close link has been reported between increasing hypertrophy and increasing diastolic dysfunction.¹⁸ The independent effect of myocardial ischemia on diastolic parameters can only be assessed by excluding patients with left ventricular hypertrophy (LVH).

Several studies have found that there are no significant differences in clinical features, ECG findings, or hemodynamic data between symptomatic and asymptomatic patients.¹⁹⁻²⁶ An alternate hypothesis claims that silent ischemia represents either less widespread ischemia or ischemia of a lower intensity.^{5,27-31} However, important problems are inherent in all of these studies. For example, none of these studies addressed the issue of patients with totally asymptomatic silent ischemia as classified by Cohn³²: patients had either angina or a prior infarction and were divided into asymptomatic and symptomatic groups based on whether angina developed during exercise tests. In addition, patients with LVH were excluded in only a few reports.²⁸⁻³⁰ Angina pectoris is a late expression of myocardial ischemia, and symptomatic ischemia in the same patients may represent more severe ischemia than asymptomatic episodes. The level of stress relative to the deficit in myocardial perfusion may result in the appearance of symptomatic episodes. Severity of ischemia is generally a fundamental factor in determining the presence or absence of cardiac pain during ischemic episodes in the same patient. However, whether or not it is sufficient to fully explain the presence of chest pain is still controversial. Furthermore, it is very important to use patients with entirely silent ischemia to elucidate the pathophysiologic characteristics of silent myocardial ischemia.

The purpose of this study was to determine hemodynamic parameters in patients with totally asymptomatic silent myocardial ischemia, and to investigate the influence of LVH on left ventricular filling dynamics in

dynamic exercise-induced silent myocardial ischemia.

METHODS

Patients

The study group consisted of a total of 20 male patients (age, 41–71 years; mean age, 55 years) with angiographically significant coronary artery lesions who were evaluated by supine leg exercise during invasive examination (Tables I and II). These patients were suspected of having coronary artery disease due to abnormal ST-segment changes at rest and/or ischemic ST-segment changes during treadmill exercise tests. These abnormalities were incidental findings on routine company medical examinations. Patients with a history of previous myocardial infarction and/or diabetes mellitus were excluded from this study. The diagnosis of a previous myocardial infarction was based on a history of an appropriate event associated with electrocardiographic and/or enzymatic changes.

The patients were divided into 2 groups of ten: group I (age, 41–71 years; mean age, 55 years) and group II (age, 46–66 years; mean age, 54 years) as shown in Table II. Group I included patients with a normal left ventricular wall thickness (posterior wall thickness of 11 mm or less) and group II included patients with LVH (posterior wall thickness of 12 mm or greater). All of the patients developed ischemic ST-segment depression in symptom-limited graded exercise tests (at least four times) in the absence of angina or its usual equivalents. These tests were performed to familiarize the patients with supine leg exercise and to avoid poor reproducibility of exercise test results. The study was approved by an appropriate institutional review committee. Each patient was informed in detail of the purpose and method of the study and gave their written informed consent.

Echocardiographic Studies

M-mode and two-dimensional echocardiograms were obtained with a cross-sectional ultrasonoscope (HP 77030A, Hewlett Packard, Andover, Massachusetts) with a 2.25 MHz transducer. Two-dimensional echocardiograms were recorded on a video system and M-mode echocardiograms were photo-

graphed on light-sensitive paper (Model TLR111, Kowa Co., Ltd., Tokyo, Japan) at a paper speed of 50 mm/s using a Honeywell 1956 strip chart recorder. Echocardiograms were obtained at the end of expiration. 12-lead ECGs were also recorded. The measurements on the echocardiograms were made by two observers (who were unaware of the patient's clinical state) from at least six consecutive cardiac cycles.

The thickness of the interventricular septum and the left ventricular posterior wall was measured at the time of the peak R wave on the ECG (end-diastole), with the ultrasound beam directed just below the tip of the anterior mitral leaflet on the M-mode echocardiogram. The thickness of the interventricular septum and the left ventricular posterior wall was measured by the Penn convention.³³ All measurements were made with a centimeter scale superimposed on the echocardiogram.

Hemodynamic Studies

A triple-lumen thermistor Swan-Ganz catheter (Baxter Healthcare Corp., Edwards Division, Santa Ana, California) was positioned percutaneously in the pulmonary artery through the brachial vein to measure cardiac output and pulmonary artery wedge pressure. The thermodilution technique was used to determine cardiac output. The curve recorded with the thermodilution cardiac output computer (model RI-5DCP, General Scanning Inc., Watertown, Massachusetts) was checked for consistency before the results were accepted as reflecting cardiac output. Irregular curves, especially during exercise, were excluded from the study. A double-thermistor catheter (model CCS/TU-GOK, Wilton-Webster Laboratories, Los Angeles, California) was placed percutaneously in the coronary sinus through the brachial vein. The distal external thermistor was advanced to the great cardiac vein, and the proximal external thermistor was positioned under fluoroscopic guidance in the coronary sinus between the ostium and the termination of the middle cardiac vein. Coronary sinus and great cardiac vein flows were calculated according to the method of Ganz *et al*³⁴ using a computer system (Thermo Flow, Goodman Co., Ltd., Nagoya, Japan). The injectate was normal saline

solution at room temperature delivered by a Harvard pump at a flow rate of 40 ml/min. Coronary sinus flow and great cardiac vein flow were recorded on a six-channel recorder (Unicorder, Nippon Denshi Kagaku, Co., Ltd., Kyoto, Japan) at a paper speed of 100 cm/min. A teflon catheter was also cannulated in the brachial artery for direct measurement of arterial pressure. A pulmonary artery wedge pressure transducer (model 746, Siemens Medical System Inc., Solna, Sweden) was placed at a zero reference midchest level.

Bicycle Ergometer Exercise Testing

All drugs were withdrawn from the patients for at least four days prior to the study. The method of invasive hemodynamic exercise testing has been reported elsewhere.³⁵ Symptom-limited bicycle ergometer (electronically braked ergometer) exercise testing was performed in patients in the supine position. The exercise end point was leg fatigue or general fatigue in all of the patients studied. The work load was begun at 150 kpm/min (25 W) and increased stepwise by 150 kpm/min at 3 min intervals. During the exercise testing, a modified 12-lead electrocardiogram³⁶ was recorded continuously. Pulmonary artery wedge pressure, arterial pressure, cardiac output, and coronary sinus flow were measured at rest, every 3 min during exercise, at peak exercise, and at 1, 3, and 6 min after exercise.

Blood Sampling

Samples of blood for oxygen saturation were simultaneously obtained from the brachial artery, the pulmonary artery, and the coronary sinus at rest, every 3 min during exercise, at peak exercise, and at 3 and 6 min after exercise. Blood oxygen saturation was determined with a hemoximeter (model ABL3, Radiometer, Copenhagen, Denmark).

Angiographic Assessment of Coronary Stenosis

Selective coronary arteriography and left ventriculography were performed in all patients on the same day after the graded exercise study using the Sones technique. Left ventricular volume in each patient was calculated by biplane cineangiography. Each

TABLE I SUMMARY OF PERTINENT CLINICAL AND ANGIOGRAPHIC FINDINGS IN PATIENTS WITH TOTALLY ASYMPTOMATIC SILENT MYOCARDIAL ISCHEMIA WITH OR WITHOUT LEFT VENTRICULAR HYPERTROPHY

Patient	Age (yr)	Sex	Coronary angiogram				Left ventricular angiogram	
			(% diameter reduction)			Collateral filling	EF (%)	Wall motion
			LAD	LCX	RCA			
Group I (without LVH)								
1	56	M	75	100	75	fair	77	normal
2	71	M	75	75	99	good	79	normal
3	52	M	0	99	0	good	84	normal
4	58	M	75	0	0	none	91	normal
5	56	M	75	0	0	none	84	normal
6	41	M	0	0	100	good	61	inferior hypokinesia
7	66	M	90	0	25	none	74	normal
8	42	M	99	75	0	fair	78	anterior hypokinesia
9	55	M	25	0	100	good	82	inferior hypokinesia
10	49	M	25	75	90	fair	73	normal
Group II (with LVH)								
1	46	M	100	0	0	fair	84	anterior hypokinesia
2	66	M	99	90	90	good	75	normal
3	51	M	100	50	99	fair	80	anterior hypokinesia
4	57	M	75	0	0	none	64	normal
5	55	M	75	0	0	none	83	normal
6	58	M	50	100	0	good	71	normal
7	52	M	75	0	99	good	78	normal
8	55	M	0	00	0	good	78	normal
9	49	M	100	90	90	good	72	normal
10	51	M	75	50	90	poor	83	normal

LVH, left ventricular hypertrophy; LAD, left anterior descending artery; LCX, left circumflex artery; RCA, right coronary artery; EF, ejection fraction; M, male; F, female.

coronary artery was viewed in multiple projections. Coronary cineangiograms were recorded on 35 mm film, and reviewed on a Tagarno projector. Coronary and left ventricular angiographic data were analyzed according to the A.H.A. Committee Report³⁷ Collateral filling of the coronary arterial branch was judged angiographically. Good filling was defined as opacification of the collaterally filled branch equal to that of vessels directly filled; poor filling was defined as just barely detectable opacifications; and fair filling was defined as being between good and poor.

Calculations

The baseline from which observed electrocardiographic changes were measured was taken from a line joining 2 consecutive P-Q junctions. The magnitude of ST-segment depression was measured using a x7 magnify-

ing glass calibrated in 10ths of a millimeter. The electrocardiographic criteria for a positive test in any lead were horizontal or downsloping ST-segment depression ≥ 0.1 mV for 0.08 seconds, or a slow upsloping ST-segment depression ≥ 0.2 mV 0.08 seconds after the J point in at least three consecutive complexes. The degree of ST changes was expressed in terms of the maximum value of ischemic ST-segment depression in any of the 12 leads recorded. The time from the start of exercise to the onset of ischemic ST-segment depression was measured and defined as ischemic threshold.

Hemodynamic variables were calculated as follows: (rate-pressure product) = (systolic blood pressure) $\times$ (heart rate); (cardiac index [L/min/m²]) = (cardiac output/body surface area); (oxygen content [vol%]) = {(oxygen saturation[%] $\times$ hemoglobin concentration [g/dl] $\times$ 1.34/100} ; (myocardial oxygen up-

TABLE II COMPARISON OF CLINICAL, ECHOCARDIOGRAPHIC, AND ANGIOGRAPHIC CHARACTERISTICS IN PATIENTS WITH OR WITHOUT LVH, AND SILENT ISCHEMIA

	Patients with Silent Myocardial Ischemia		P value
	Group I (without LVH)	Group II (with LVH)	
Patients (no.)	10	10	
Age (yr)			
Mean $\pm$ SD	55 $\pm$ 9	54 $\pm$ 6	NS
Range	41 to 71	46 to 66	
Number of diseased vessels			NS*
1 vessel	6	5	
2 vessels	2	3	
3 vessels	2	2	
Critically stenosed vessels ($>75\%$ narrowing)			NS*
LAD	6	8	
LCX	5	4	
RCA	5	5	
Collateral filling			NS*
good	4	5	
fair	3	2	
poor	0	1	
none	3	2	
EF at rest (%)			
Mean $\pm$ SD	78 $\pm$ 8	77 $\pm$ 7	NS
Range	61 to 91	64 to 84	
Left ventricular anatomy			
PW thickness (mm)			
Mean $\pm$ SD	9 $\pm$ 1	15 $\pm$ 2	$p < 0.001$
Range	8 to 11	12 to 18	
IVS thickness (mm)			
Mean $\pm$ SD	9 $\pm$ 1	14 $\pm$ 2	$p < 0.001$
Range	(7 to 10)	(10 to 16)	

EF, ejection fraction; LAD, left anterior descending artery; LCX, left circumflex artery; RCA, right coronary artery; PW, posterior wall; IVS, interventricular septum; LVH, left ventricular hypertrophy; NS, not significant

*Mann-Whitney Test

take [ml/min]) = (arterial oxygen content - coronary sinus oxygen content) $\times$ (coronary sinus flow/100).

Statistics

Statistical analysis was carried out by the unpaired t test: a p value of less than 0.05 was considered to be statistically significant. The extent of coronary artery disease (including the number of diseased vessels and critically stenotic vessels) in the 2 groups was compared using the Mann-Whitney test.

Pulmonary artery wedge pressure and coronary sinus flow during exercise testing in group I were compared with those in group

II using a two-way analysis of variance. In addition to the two-way analysis of variance, Scheffe's test was used to compare the 2 groups at each point of exercise testing. All of the values in the text and Tables represent the mean $\pm$ SD.

RESULTS

Clinical, Echocardiographic, and Angiographic Findings (Tables I and II)

The 10 patients in group I had totally asymptomatic silent myocardial ischemia without LVH, while the 10 patients in group II had the same type of silent myocardial

TABLE III HEMODYNAMIC CHANGES DURING EXERCISE IN PATIENTS WITH OR WITHOUT LVH, AND SILENT ISCHEMIA

	Patients with Silent Myocardial Ischemia		<i>p</i> value
	Group I (without LVH)	Group II (with LVH)	
<i>Exercise duration (sec)</i>			
1 mm ST depression	370±139	354±151	NS
Peak exercise	566±122	550±142	NS
<i>Work load attained (watts)</i>			
1 mm ST depression	58±24	58±24	NS
Peak exercise	83±17	80±20	NS
<i>HR (beats/min)</i>			
Rest	71±16	67±12	NS
1 mm ST depression	116±17	105±17	NS
Peak exercise	132±20	118±19	NS
<i>ST depression (mm)</i>			
Peak exercise	0.12±0.01	0.15±0.02	<0.01
<i>SBP (mmHg)</i>			
Rest	150±22	173±25	<0.05
1 mm ST depression	193±38	212±31	NS
Peak exercise	202±35	221±32	NS
<i>RPP (×10²)</i>			
Rest	108±33	114±22	NS
1 mm ST depression	230±81	225±65	NS
Peak exercise	269±79	262±63	NS
<i>PAWP (mmHg)</i>			
Rest	4±2	7±4	NS
Peak exercise	11±3	19±7	<0.01
<i>CI (L/min/m²)</i>			
Rest	3.0±0.6	2.8±0.5	NS
Peak exercise	7.2±1.6	6.1±1.2	NS
<i>CSF (ml/min)</i>			
Rest	101±38	117±67	NS
Peak exercise	263±93	294±68	NS
<i>MVO₂ (ml/min)</i>			
Rest	10.3±1.2	10.6±1.4	NS
Peak exercise	27.8±3.9	28.8±5.5	NS

Values are expressed as means values ±SD

HR, heart rate; SBP, systolic blood pressure; RPP, rate-pressure product; PAWP, pulmonary artery wedge pressure; CI, cardiac index; CSF, coronary sinus flow; MVO₂, myocardial oxygen uptake; LVH, left ventricular hypertrophy; NS, not significant

ischemia with LVH (mainly due to essential hypertension).

Among the 20 patients studied, 11 had single vessel involvement, 5 had 2-vessel disease, and 4 had 3-vessel disease. Good collateral filling by coronary angiograms was observed in 9 patients, fair collateral filling was observed in 5 patients, and poor collateral filling was found in 1 patient. Five patients had no collateral filling. Left ventricular ejection fraction at rest ranged from 61% to 91% (mean, 77±7%).

Both groups were comparable in age, sex,

left ventricular ejection fraction at rest, and extent of coronary artery disease as defined by the number of diseased vessels, critically stenotic vessels, and collateral filling. Patients in the 2 groups also had comparable histories of diabetes mellitus and myocardial infarction.

Left ventricular posterior wall thickness ranged from 8 mm to 11 mm (mean, 9±1 mm) in group I, and from 12 mm to 18 mm (mean, 15±2 mm) in group II. These values were significantly different ($p<0.001$).

Fig.1. Changes in pulmonary artery wedge pressure (PAWP) of patients with or without left ventricular hypertrophy (LVH) during supine leg exercise. Values are expressed as mean $\pm$ SEM. Statistical analyses were carried out by a 2-way analysis of variance and Sheffe's test.

Functional Parameters during Supine Leg Exercise Tests (Table III and Fig. 1)

The exercise end-point in all of the patients studied was leg fatigue or general fatigue, and all of the patients developed significant ischemic ST-segment depression during testing. The mean ST-segment depression was 0.12 ± 0.01 mV in group I and 0.15 ± 0.02 mV in group II ($p < 0.01$). There were no significant differences in exercise heart rate, work load attained, time to onset of 1 mm ST-segment depression, or time to peak exercise between the 2 groups.

Pulmonary artery wedge pressure at rest ranged from 1 mmHg to 7 mmHg (mean, 4 ± 2 mmHg) in group I, and from 1 mmHg to 15 mmHg (mean, 7 ± 4 mmHg) in group II. This difference was not statistically significant. Pulmonary artery wedge pressure at peak exercise in group I (range 6 mmHg to 15 mmHg; mean, 11 ± 3 mmHg) was significantly less than that in group II (range 13 mmHg to 35 mmHg; mean, 19 ± 7 mmHg) ($p < 0.01$). Only 2 patients in group II had pulmonary artery wedge pressure less than 15 mmHg at peak exercise.

Coronary sinus blood flow in group I increased from 101 ± 38 ml/min at rest to 263 ± 93 ml/min at peak exercise, and from 117 ± 67 ml/min at rest to 294 ± 68 ml/min at peak exercise in group II. There were no significant differences between the 2 groups.

Myocardial oxygen uptake in group I increased from 10.3 ± 1.2 ml/min at rest to 27.8 ± 3.9 ml/min at peak exercise, and from 10.6 ± 1.4 ml/min at rest to 28.8 ± 5.5 ml/min at peak exercise in group II. These values were not significantly different between the two groups.

DISCUSSION

The precise pathophysiologic mechanisms which underlie the differences between symptomatic and silent ischemic episodes are not clearly understood, although extensive studies have been carried out in this field. However, there were important problems inherent in each of these studies. For example, none of these studies addressed the issue of patients with totally asymptomatic silent myocardial ischemia as classified by Cohn³². Furthermore, most of these studies included patients with LVH, which may induce left ventricular diastolic dysfunction¹⁸. In the present study, patients with totally asymptomatic silent myocardial ischemia were divided into two groups on the basis of LVH. Patients in the two groups were comparable in age, sex, left ventricular systolic function at rest, and extent of coronary artery disease. Patients with a history of prior myocardial infarction were excluded from this study, since hemodynamic responses during

exercise could be affected by preexisting myocardial scarring of the left ventricle. Patients in both groups tolerated a similar degree of stress, which was expressed in terms exercise duration, exercise work load and myocardial oxygen uptake, which suggests that the patients in both groups had the same work capacity.

Coronary Anatomy in Patients Without Chest Pain

Our results indicate that asymptomatic myocardial ischemia can occur even in patients with multivessel coronary artery disease. In addition, exercise-induced chest pain may be a nonspecific and insensitive finding in a patient population primarily with one-vessel disease, as reported by Mahmarian et al.²⁵ Therefore, the extent of angiographically confirmed coronary artery stenosis should not be regarded as a direct indicator of the severity of exercise-induced myocardial ischemia.

Ventricular Filling Characteristics

Myocardial ischemia with chest pain induced by dynamic exercise is associated with abnormal ventricular function characterized by a marked increase in left ventricular filling pressure.¹⁰⁻¹² The mechanism of this increase remains controversial. Several studies¹³⁻¹⁶ have shown that angina-related increased left ventricular filling pressure reflects both reduced left ventricular diastolic distensibility and systolic dysfunction. Recently, decreased myocardial distensibility has been shown to contribute significantly to increased left ventricular diastolic pressure seen during angina pectoris.^{17,38} The exercise-induced increase in left ventricular filling pressure of patients who had totally asymptomatic silent myocardial ischemia was very mild in the absence of LVH. In contrast, the same type of silent myocardial ischemia in association with LVH resulted in severe increases in left ventricular filling pressure during dynamic exercise. In addition, we have previously shown that patients with symptomatic ischemia developed severe exercise-induced increases in left ventricular filling pressure.^{35,39,40}

Therefore, we conclude that the exercise-induced increase in left ventricular filling pressure is very mild, which may lead to less

ischemia in patients with totally asymptomatic silent myocardial ischemia.

Myocardial Ischemia and LVH

Several factors may be responsible for myocardial ischemia in patients with LVH. A transmural gradient of coronary blood flow is established in LVH, with reduced flow in the subendocardial layers⁴¹ which is accentuated by pacing⁴² and exercise.⁴³ Although total myocardial blood flow is increased in LVH, the flow per 100 g is significantly reduced⁴⁴ because of decreased coronary vascular reserve⁴⁵ and possibly disease of the small vessels.⁴⁶ Coexistence of these processes with significant coronary stenosis may induce severely abnormal left ventricular filling dynamics during exercise-induced ischemic episodes, which in turn cause marked ST-segment depression. However, this elevated filling pressure is not necessarily sufficient to produce chest pain.

There is evidence to suggest that the hypertrophied heart may be especially likely to develop impaired diastolic function in response to ischemia or hypoxia, as compared to the nonhypertrophied heart.^{47,48} This observation has been corroborated in a model that simulates pressure overload hypertrophy with coexisting coronary artery disease. It has been shown in this model that isolated blood-perfused hypertrophied hearts develop more severe diastolic dysfunction in response to brief demand ischemia.⁴⁹

The mechanisms responsible for the increased occurrence of diastolic dysfunction in the hypertrophied heart in response to brief demand ischemia or hypoxia are not completely understood. Hypertrophied myocardium appears to be characterized by intrinsic alterations of cytosolic calcium regulation. This is evident as a marked prolongation of the calcium transient⁵⁰ that in part is related to alterations of the calcium uptake function of the sarcoplasmic reticulum.⁵¹ A prolongation of cytosolic calcium availability at the level of the myofilaments during systole may be adaptive during aerobic conditions and facilitate sustained force development against an increased afterload. However, this intrinsic alteration in intracellular calcium regulation may place the hypertrophied myocardium in jeopardy with a profound impairment of relaxation when the

control of diastolic calcium homeostasis by the sarcoplasmic reticulum and sarcolemmal pumps is further depressed by brief periods of ischemia.⁵²

Mechanisms of Ischemic Cardiac Pain

The mechanisms of cardiac pain in myocardial ischemia are not precisely known. Angina pectoris is a late expression of myocardial ischemia. In the same patient, impaired left ventricular relaxation and increased left ventricular filling pressure always precede chest pain, and symptomatic ischemia may represent more severe ischemia than asymptomatic episodes. Stretching of the ventricular wall might be the stimulus responsible for anginal pain.⁵³ However, our study clearly demonstrates that although patients with totally asymptomatic silent myocardial ischemia and LVH had severe elevation of left ventricular filling pressure, which could potentially result in stretching of the left ventricular wall during exercise, they did not feel chest pain. Therefore, distention of the ventricular wall does not necessarily cause chest pain, as previously reported.⁵⁴

In summary, ischemic episodes which caused marked ST-segment depression and severely increased left ventricular filling pressure did not provide adequate stimuli to produce chest pain in patients with LVH and significant coronary artery stenosis. Therefore, other factors, including endogenous adenosine,^{55,56} the patient's pain perception threshold,⁵⁷⁻⁵⁹ and central transmission of painful stimuli⁶⁰ must be considered as causes of cardiac pain.

Study Limitations

In this study, we did not compare hemodynamic changes in patients with and without symptomatic angina. It is usually important to compare these two groups. However, a marked increase in left ventricular filling pressure in exercise-induced ischemia with chest pain has been fully recognized.^{10-17,35,39,40} Furthermore, it may be difficult to distinguish characteristics of patients with different exercise end-points.

CONCLUSIONS

Based on the present results, we conclude that totally asymptomatic silent myocardial

ischemia can exist in the presence of normal or mildly abnormal left ventricular filling dynamics during ischemic episodes which cause marked ST-segment depression in the presence of greatly increased myocardial oxygen demand. In addition, patients with LVH can have severely abnormal left ventricular filling dynamics during exercise without ischemic cardiac pain. Severity of ischemia and/or stretching of the ventricular wall may be necessary, but not sufficient, for the occurrence of chest pain.

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