Exercise Induced Ventricular Arrhythmias

Angiographic Correlation with the Severity of Coronary Artery Disease

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SUMMARY

We correlated the incidence and degree of exercise induced ventricular arrhythmias (EIVA) with the angiographic severity of coronary artery disease (CAD) in 162 patients with a history of stable effort angina, all showing a positive exercise stress test for myocardial ischemia and a $\geq 70\%$ stenosis of a major coronary artery. Patients were grouped according to the following criteria: presence of electrocardiographic evidence of old transmural myocardial infarction (MI), number of significant coronary stenoses and number of left ventricular (LV) areas showing abnormal segmental wall motion (ASWM).

The incidence of EIVA in patients with multivessel CAD was higher than in patients with single vessel CAD, but this difference was not statistically significant. The number of LV areas with ASWM was better correlated with the frequency of EIVA, which was 20.0% in patients with normal LV wall motion, 31.2% in patients with 1 area of ASWM, 54.0% in patients with 2 areas of ASWM ($p < 0.005$ vs normal LV wall motion), 74.1% in patients with 3 or more areas of ASWM ($p < 0.001$ vs normal LV wall motion and 1 area of ASWM), and 81.8% in patients with LV aneurysm ($p < 0.001$ vs normal LV wall motion and 1 area of ASWM, $p < 0.005$ vs 2 areas of ASWM). Patients with old MI showed a significantly higher incidence of EIVA than those without MI ($p < 0.001$), but this difference was due to the more severe LV asynergy in the MI group.

In conclusion, our results show that, in a selected population

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of patients with CAD, the incidence of EIVA correlates better with the extent of LV segmental wall motion abnormalities than with the number of diseased coronary arteries or the presence of an old transmural MI.

Additional Indexing Words:

Exercise Stable angina on effort

VENTRICULAR arrhythmias are important prognostic indicators of sudden¹⁾⁻⁵⁾ and non-sudden⁶⁾ death in patients with coronary artery disease (CAD). However, since mortality in these patients is mostly influenced by the degree of left ventricular (LV) functional impairment,⁷⁾ ventricular arrhythmias are likely to reflect only the severity of ischemic damage to the left ventricle, together with the number of coronary arterial narrowings.⁸⁾ Exercise induced ventricular arrhythmias (EIVA) have been observed both in patients with CAD and in normal subjects⁹⁾⁻¹²⁾; thus their clinical significance and prognostic implications are still controversial. EIVA are generally observed less frequently in normal subjects than in patients with CAD, and among the latter, are more easily found in those with more advanced LV functional impairment.⁹⁾⁻¹⁴⁾ However, it is still controversial whether the presence and severity of EIVA correlate better with the severity of coronary arterial narrowings, the extent of LV contraction abnormalities, or the presence of old myocardial infarction (MI). Furthermore, a correlation between EIVA and the degree of myocardial ischemia demonstrated in a recent study¹³⁾ was not confirmed by others.^{10),12)} The present study was thus aimed to better delineate the clinical significance of EIVA, through correlations with the angiographic severity of CAD and a history of MI.

MATERIALS AND METHODS

One hundred and sixty-two patients who had a positive exercise stress test and significant coronary stenosis at coronary arteriography in our Institute constituted our study group. All patients had a history of stable angina on effort. We excluded from the study patients with severe resting ventricular arrhythmias, since these constitute a common contraindication to performing an exercise stress test.¹⁵⁾ Also excluded were patients with valvular disease, cardiomyopathy, conduction defects, and systemic hypertension.

Exercise stress test:

All patients underwent an exercise stress test in a sitting position with a Sasme Ergo 2 bicycle ergometer. Patients exercised in the early morning

after an overnight fast; all drugs had been discontinued at least 48 hours before the test. The initial load of 50 watts was increased by 20 watts every 2 min, using the maximal predicted heart rate as a target end point. CM 4, 5, and 6 leads were continuously monitored; electrocardiographic recordings were obtained at rest, each minute during the exercise period, at peak exercise and each minute during a 5-min recovery period (Avionics 3000). Resting ventricular arrhythmias were ruled out by means of a baseline 12-lead electrocardiogram, followed by a 3-min period of continuous electrocardiographic monitoring before the start of exercise. Positive criteria of ischemia were: a 1 mm ST segment depression 60 msec from the J point, if the ST segment was horizontal or downsloping; a 1.5 mm ST segment depression 80 msec from the J point, if the ST segment was upsloping.¹⁵⁾ ST segment depression was continuously monitored during the test using an Avionics ST computer. The criterion for interrupting the exercise testing was the development of significant ST segment depression, as defined above, whether or not it was accompanied by angina.

EIVA were defined as those arrhythmias appearing during the exercise or in the recovery period. Their severity was graded according to the following classification of Lown and Wolfe¹⁶⁾ as modified by Tilkian¹⁷⁾: 0: no arrhythmias; 1: rare (less than 1 in 100 beats) premature ventricular complexes (PVCs); 2: frequent (more than 1 in 100 beats) PVCs; 3: multiform PVCs; 4: PVCs in couplets; 5: early PVCs (R on T phenomenon); 6: ventricular tachycardia (VT); 7: ventricular fibrillation.

Angiographic and hemodynamic data:

Pressures were measured through fluid filled catheters and Statham P-23-Db transducers on a OTE multichannel recorder. Cardiac output was measured by thermodilution. Maximal rate of rise of LV pressure (LV dP/dt max) was obtained by an intergration channel. Coronary arteriography was performed by the Sones technique.¹⁸⁾ Several selective coronary injections were performed in multiple oblique projections. Left ventriculography was performed both in the right and left oblique projections using an injection of 45 cc of 76% Urografin at 15 cc/sec in the LV with a Viamonte-Hobbs injector. Angiographic images were recorded by a General Electric cine-angiographic system equipped with a Fluoricon 300 image intensifier. LV angiograms were divided into the following segments: antero-basal, antero-lateral, apical, diaphragmatic, postero-basal, postero-lateral, and septal. Evaluation of LV segmental wall motion was performed subjectively since it has been demonstrated that qualitative evaluation of the degree of LV asynergy compares well with quantitative angiography.¹⁹⁾ LV wall motion was defined as normal in cases of normal segmental contraction

during systole or asynergic in cases of hypokinetic, akinetic or diskynetic contraction of one or more LV segments.

Left ventriculograms were evaluated independently by three expert angiographers unaware of the results of the exercise test or the clinical data.

The severity of impairment of LV contraction was scored according to the number of asynergic segments, as in previous studies.²⁰⁾ If the ventriculographic score given by the three observers was not the same, the score assigned by two of them was considered. The diagnosis of LV aneurysm (LVAn) was made angiographically according to the criteria proposed by Loop et al.²¹⁾ Severity of CAD was expressed according to significant (narrowing $\geq 70\%$ of lumen diameter) involvement of one, two or three major coronary vessels (left anterior descending coronary artery, or large diagonals; circumflex coronary artery, either main stem, large obtuse marginal or postero-lateral branch; right coronary artery, main stem or posterior descending branch). Significant stenoses of smaller branches were not considered in the evaluation. Main left coronary artery (MLCA) lesions were considered separately. Patients were subdivided in groups according to three criteria: 1) the number of significantly involved coronary arteries; 2) the number of LV areas with abnormal wall motion (ASWM); 3) the presence or absence of electrocardiographic evidence of old transmural MI, evaluated on the basis of commonly accepted electrocardiographic criteria.²²⁾

Subdivision according to number of coronary stenoses:

The first group (1-V) was composed of 30 patients, 23 males and 7 females, aged 38 to 62 years (mean 53), with significant stenosis of only one major coronary artery. Eleven of these patients (36.6%) had electrocardiographic evidence of old MI and 15 (50.0%) demonstrated ASWM. The second group (2-V) was composed of 58 patients, 49 males and 9 females, aged 39 to 65 years (mean 57), with two coronaries significantly involved. Thirty-two (55.1%) of these patients presented electrocardiographic signs of old MI and 45 (77.5%) ASWM. Fifty-nine patients, 52 males and 7 females, aged 44 to 66 years (mean 58) constituted the third group (3-V). All had three coronaries significantly involved. Forty-two of these patients (71.1%) had electrocardiographic evidence of old MI and 51 (86.4%) demonstrated ASWM. The fourth group (MLCA) was composed of 15 patients, 14 males and 1 female, aged between 49 and 64 years (mean 57), with significant stenosis of the MLCA. Eleven of these patients (73.3%) had associated significant disease of two or three major coronary arteries. Electrocardiographic signs of old MI were present in 10 of these patients (66.6%) and ASWM in 11 (73.3%).

Subdivision according to the severity of LV asynergy:

The first group (0-ASWM) was composed of 40 patients with normal LV wall motion, 15 of them (37.5%) with single, 13 (32.5%) with double, 8 (20.0%) with triple vessel CAD, and 4 (10.0%) with MLCA disease. Thirteen of these patients (32.5%) had electrocardiographic signs of old transmural MI. The second group (1-ASWM) was composed of 32 patients, 5 of them (15.6%) with single, 13 (40.6%) with double, 10 (31.2%) with triple vessel CAD, and 4 (12.5%) with MLCA disease, all showing asynergic contraction of only one LV segment at left ventriculography. Thirteen of these patients (40.6%) presented electrocardiographic signs of old transmural MI. Thirty-seven patients constituted the third group (2-ASWM), all showing asynergic contraction of 2 LV segments at left ventriculography. Of these patients, 6 (16.2%) had single, 13 (35.1%) double, 16 (43.2%) triple vessel CAD, and 2 (5.4%) had MLCA disease. Twenty-three of these patients (62.1%) had electrocardiographic evidence of previous transmural MI. The fourth group (3-ASWM) was composed of 31 patients with 3 or more areas of asynergy at left ventriculography. Two of these patients (6.4%) had single, 12 (38.7%) double, 14 (45.1%) triple vessel CAD, and 3 patients (9.6%) MLCA disease. Old transmural MI was present in 24 of these patients (77.4%). The fifth group (LVAn) consisted of 22 patients with LVAn, 2 of whom (9.0%) had single, 8 (36.4%) double, 10 (45.5%) triple vessel CAD, and 2 (9.0%) MLCA disease. All patients (100%) had electrocardiographic evidence of old transmural MI.

Subdivision according to presence of old transmural MI:

Ninety-five of the 162 patients (58.6%) had electrocardiographic evidence of old transmural MI. Normal LV segmental wall motion was observed in 13 (13.6%), 1 area of ASWM in 13 (13.6%), 2 areas of ASWM in 23 (24.2%), 3 areas of ASWM in 24 patients (25.2%), and LVAn in 22 patients (23.1%). Infarct location was as follows: inferior in 59 (62.1%), antero-septal in 21 (22.1%), antero-lateral in 5 (5.2%), and anterior plus inferior in 10 patients (10.5%). Of the 67 patients (41.4%) without electrocardiographic signs of old MI, 27 (40.2%) had a normal left ventriculogram, 19 (28.3%) 1 area of ASWM, 14 (20.8%) and 7 (10.4%) 2 and 3 areas of ASWM, respectively.

Furthermore, we evaluated the incidence of EIVA during the exercise and recovery periods, the heart rate at the time of appearance of EIVA and the clinical characteristics of patients with EIVA during the exercise and recovery period. Finally, we tried to correlate EIVA with ST segment depression occurring during exercise or in the recovery period. Statistical analysis was performed comparing the incidence of EIVA among various

Table I. Incidence of Exercise Induced Ventricular Arrhythmias and of Abnormal Left Ventricular Segmental Wall Motion in Patients Subdivided According to the Severity of Coronary Artery Disease

Group	EIVA		ASWM	
	No.	Pts %	No.	Pts %
1-V	11/30	(36.6)	15/30	(50.0)
2-V	28/58	(48.2)	45/58	(77.5)
3-V	32/59	(54.2)	51/59	(86.4)
MLCA	8/15	(53.3)	11/15	(73.3)
Total	79/162	(48.7)	122/162	(75.3)

Abbreviations: EIVA=exercise induced ventricular arrhythmias; ASWM=abnormal segmental wall motion; 1-V, 2-V, and 3-V=patient groups with single, double, and triple vessel CAD, respectively; MLCA=patient group with main left coronary artery lesions.

Table II. Incidence of Exercise Induced Ventricular Arrhythmias in Patients with Coronary Artery Disease, Subdivided by the Severity of Left Ventricular Asynrgy

Group	0-ASWM		1-ASWM		2-ASWM		3-ASWM		LVAn		Total	
	No.	Pts %	No.	Pts %	No.	Pts %	No.	Pts %	No.	Pts %	No.	Pts %
1-V	2/15	(13.3)	1/5	(20.0)	4/6	(66.6)	2/2	(100)	2/2	(100)	11/30	(36.6)
2-V	3/13	(23.0)	4/13	(30.7)	6/13	(46.1)	8/11	(72.7)	7/8	(87.5)	28/58	(48.2)
3-V	2/8	(25.0)	3/10	(30.0)	9/16	(56.2)	11/15	(73.3)	7/10	(70.0)	32/59	(54.2)
MLCA	1/4	(25.0)	2/4	(50.0)	1/2	(50.0)	2/3	(66.6)	2/2	(100)	8/15	(53.3)

Abbreviations: 0-ASWN=normal left ventricular contraction; 1-2-3 ASWN=presence of one, two, three or more asynrgic left ventricular segments, respectively; LVAn=left ventricular aneurysm; other abbreviations as in Table I.

subgroups using the Fischer test.²³⁾ Hemodynamic data were compared using the t test for unpaired samples.²³⁾

RESULTS

Seventy-nine of 162 patients (48.7%) showed EIVA. Table I illustrates the incidence of EIVA and of ASWM in patients subdivided according to severity of CAD. No significant differences were found in EIVA incidence among angiographic groups.

Incidence and severity of EIVA in patients of group 1-V, 2-V, 3-V, and MLCA disease are detailed in Table II. While EIVA were present in 11 of 30 group 1-V patients (36.6%), they were observed in 9 of the 15 patients in this group (60.0%) who showed any degree of ASWM. Of the 58 patients of the 2-V group, 28 (48.2%) showed EIVA; of these 28 patients, only 3 (10.7%) had normal LV wall motion (Table II). The most severe arrhythmias were observed only in patients with ASWM: 1 patient showed a short run of

Table III. Incidence of Exercise Induced Ventricular Arrhythmias in Patients with and without Old Myocardial Infarction, Subdivided According to the Presence and Severity of Abnormal Left Ventricular Wall Motion

Group	MI		no MI	
	No.	Pts %	No.	Pts %
0-ASWM	3/13	(23.0)	5/27	(18.5)
1-ASWM	4/13	(30.7)	6/19	(18.5)
2-ASWM	14/23	(30.7)	6/14	(42.8)
3-ASWM	18/24	(75.0)	5/7	(71.4)
LVA _n	18/22	(81.8)	—	—
Total	57/95	(60.0) [*]	22/67	(32.8)

^{*} Differs from no MI group at $p < 0.005$.

Abbreviation: MI and no MI = patients with and without old myocardial infarction, respectively; other abbreviations as in Tables I and II.

Table IV. Incidence of Exercise Induced Ventricular Arrhythmias in Coronary Population, Subdivided by Presence and Extent of Left Ventricular Asynergy

Group	No. Pts	EIVA	
		Total	%
0-ASWM	40	8/40	(20.0)
1-ASWM	32	10/32	(31.2)
2-ASWM	37	20/37	(54.0) [°]
3-ASWM	31	23/31	(74.1) [§]
LVA _n	22	18/22	(81.8) [^] [⧫]

[°] Differs from 0-ASWM at $p < 0.005$.

[§] Differs from 0-ASWM and from 1-ASWM at $p < 0.001$.

[^] Differs from 0-ASWM and from 1-ASWM at $p < 0.001$.

[⧫] Differs from 2-ASWM at $p < 0.005$.

Abbreviations as in Tables I and II.

spontaneously resolved VT and 2 patients showed R on T phenomenon.

Thirty-two of the 59 patients of the 3-V group (54.2%) showed EIVA, which, as in the other groups, were frequent in patients with ASWM (Table II). Two patients had an episode of VT, 1 with 3-ASWM and 1 with LVA_n; 1 patient with 2-ASWM exhibited R on T phenomenon. Eight of the 15 patients with MLCA disease (53.3%) had EIVA; only 1 of these 8 (12.5%) showed normal LV wall motion (Table II). The most severe arrhythmias (score 4) were observed in 4 of the 5 patients with ASWM, 2 with 3-ASWM and 2 with LVA_n.

Fifty-seven of the 95 patients with electrocardiographic evidence of old MI (60.0%) and 22 of the 67 patients with no electrocardiographic evidence of old MI (32.8%) showed EIVA ($p < 0.005$) (Table III).

Abnormal segmental wall motion was present in 82/95 (86.3%) of pa-

Table V. Hemodynamic Findings in the Coronary Population, Subdivided by the Number of Diseased Vessels

Group	No. Pts	LVEDP mmHg	CI L/min/M ²	LV dP/dt max mmHg/sec
1-V	30	12.4±2.5	3.3±.44	2060±644
2-V	58	14 ±5.2	3.2±. 8	1811±683
3-V	59	16.1±6.7 ^	2.9±.82 ^	1752±598 ^
MLCA	15	16.5±6.5°	2.9±.47°	1741±547

^ Difference from 1-V at p<0.005 (LVEDP), p<0.01 (CI) and p<0.05 (LV dP/dt max).

° Difference from 1-V at p<0.005 (LVEDP) and p<0.01 (CI).

Hemodynamic values expressed as Mean±Standard Deviation of the Mean.

Abbreviations: LVEDP=left ventricular end-diastolic pressure; CI=cardiac index; LV dP/dt max=maximal rate of rise of left ventricular (LV) pressure; other abbreviations as in Table I.

Table VI. Hemodynamic Findings in the Coronary Population, Subdivided by Presence and Extent of Left Ventricular Asynergy

Group	No. Pts	LVEDP mmHg	CI L/min/M ²	LV dP/dt max mmHg/sec
0-ASWM	40	13.0±4.2	3.4±.64	2150±602
1-ASWM	32	14.8±5.4	3.0±. 9	1930±751
2-ASWM	37	16.5±8.8 ^	2.7±. 5 ^	1715±417 ^
3-ASWM	31	19.4±6.8 ^°	2.4±. 5 ^°	1550±556 ^°
LVA _n	22	18.5±5.9% [°]	2.4±. 3% [°]	1560±480 ^°

^ Differs from 0-ASWM at p<0.025 (LVEDP) and at p<0.001 (CI and LV dP/dt max).

° Differs from 0-ASWM at p<0.001.

° Differs from 2-ASWM at p<0.005 (LVEDP), p<0.001 (CI) and p<0.05 (LV dP/dt max).

% Differs from 0-ASWM at p<0.001.

[°] Differs from 2-ASWM at p<0.02 (LVEDP), p<0.005 (CI) and p<0.05 (LV dP/dt max).

Hemodynamic values expressed as Mean±Standard Deviation of the Mean.

Abbreviations as in Tables II and V.

tients with old MI and in 40/67 (59.7%) of patients without MI (p<0.001). The incidence of EIVA was correlated with the severity of impairment of LV contraction, both in patients with and without old transmural MI. MI location had no bearing on the frequency of EIVA.

The relationship between EIVA and the severity of ASWM is illustrated in Table IV. EIVA was present in 8 of the 40 patients of the 0-ASWM group (20.0%) and in 10 of the 32 patients of the 1-ASWM group (31.2%), but this difference was not statistically significant. EIVA was observed in 20 of the 37 patients of the 2-ASWM group (54.0%), in 23 of the 31 patients of the 3-ASWM group (74.1%), and in 18 of the 22 patients with LVA_n (81.8%). Differences between 0-ASWM group and 2- 3-ASWM groups were statistically significant (p<0.005 and p<0.001, respectively), as were those between 1-ASWM and 3-ASWM groups (p<0.001). The incidence of EIVA

Table VII. Hemodynamic Findings in the Coronary Population, Subdivided by the Presence or Absence of Old Myocardial Infarction

Group	No. Pts	LVEDP mmHg	CI L/min/M ²	LV dP/dt max mmHg/sec
no MI	67	12.1±7	3.4±.9	2130±640
MI	95	16.5±5.5°	2.8±.7°	1760±690°

° Differs from no MI at $p < 0.001$.

Abbreviation as in Tables III and V.

Table VIII. Angiographic Findings in Patients with Coronary Artery Disease Showing Ventricular Arrhythmias during Exercise or during the Recovery Period

	Exercise No. Pts %	Recovery No. Pts %
Coronary artery disease		
1-V	5/31 (16.1)	6/48 (12.5)
2-V	10/31 (32.2)	18/48 (37.5)
3-V	14/31 (45.2)	18/48 (37.5)
MLCA	2/31 (6.5)	6/48 (12.5)
Ventriculographic score		
0-ASWM	5/31 (16.1)	3/48 (6.2)
1-ASWM	3/31 (9.7)	7/48 (14.6)
2-ASWM	8/31 (25.8)	12/48 (25.0)
3-ASWM	9/31 (29.0)	14/48 (29.2)
LVA _n	6/31 (19.4)	12/48 (25.0)

Abbreviations as in Tables I and II.

in patients with LVA_n was significantly higher than in patients with 0-ASWM ($p < 0.001$), 1-ASWM ($p < 0.001$) and 2-ASWM ($p < 0.005$).

Tables V, VI, and VII show the principal hemodynamic data (LV end-diastolic pressure, cardiac index, and LV dP/dt max) in our patients subdivided according to the number of diseased vessels (Table V), the degree of LV contraction impairment (Table VI), and the presence of old MI (Table VII). Patients with 3-vessel CAD and MLCA disease showed a more compromised hemodynamic status than did single vessel CAD patients. In patients with 2-ASWM, 3-ASWM, and LVA_n LV end-diastolic pressure was higher and cardiac index and LV dP/dt max were lower than in those patient with 0-ASWM. Furthermore, the hemodynamic status was more compromised in patients with 3-ASWM and LVA_n compared with those with 1-ASWM. Patients with 3-ASWM and LVA_n presented the highest LV end-diastolic pressure and the lowest cardiac index and LV dP/dt max. Finally, patients with MI had higher LV end-diastolic pressure and lower cardiac index and LV dP/dt max than did patients without MI.

Only 15 patients (9.2%) exhibited ventricular arrhythmias at rest before the initiation of exercise. These arrhythmias were mild enough not to contraindicate the test. In 7 of these 15 patients the arrhythmias disappeared during exercise; 4 of these 7 patients had 3-vessel CAD. Of the other patients, in 3 ventricular arrhythmias increased in severity and in 5 they remained unchanged during stress test and in the recovery period. In 31 patients, including 8 patients with ventricular arrhythmias at rest, ventricular arrhythmias were observed during the course of the exercise test at heart rate of 109 ± 11 beats/min (mean $\pm$ S.D.). In 48 patients ventricular arrhythmias developed during the recovery period at heart rate of 93 ± 20 beats/min (mean $\pm$ S.D.); 35 of these 48 developed EIVA between the first and the fourth minute of the recovery period. These patients did not show a significantly higher incidence of multiple vessel CAD or of ASWM (Table VIII).

We did not find a temporal correlation between EIVA and ST segment depression on the electrocardiogram. In 25 patients arrhythmias preceded electrocardiographic signs of ischemia, in 6 of these disappearing when ST segment depression occurred. In 48 patients arrhythmias occurred in the recovery period when ST segment depression had already developed.

DISCUSSION

Ventricular arrhythmias are important prognostic indicators of sudden death.¹⁾⁻⁵⁾ Since the angiographic severity of coronary arterial narrowing⁶⁾ and impairment of left ventricular contraction⁷⁾ are the main determinants of mortality, sudden or non-sudden, in patients with CAD, it is conceivable that they can be also reflected in those ventricular arrhythmias induced by exercise. A better understanding of the clinical significance of EIVA could be an important contribution to the prevention of sudden death, if this would lead to the identification of high risk patients.

The angiographic characteristics of our patients were largely influenced by the methods of selection adopted in our study. Since a positive exercise stress test was the prerequisite for inclusion, our study contained a higher than normal incidence of patients with multivessel CAD, since this angiographic characteristic is more frequently associated with a positive exercise stress test.²⁴⁾⁻²⁶⁾ This also explains the relative high incidence of ASWM in our population.

In agreement with other studies^{27), 28)} only 13.6% of patients with transmural MI had normal LV wall motion. However, since the total number of patients with normal LV wall motion in our population is small, and since the number of patients with MI is relatively large, it is not surprising to find

a high incidence (32.5%) of old MI in patients with normal LV wall motion. The high frequency (59.7%) of ASWM in patients with no electrocardiographic evidence of transmural MI reflects the prevalence in this group of patients with multivessel disease; this percentage, however, is not far from that reported in other studies.²⁷⁾ Other authors have demonstrated that the incidence of EIVA in patients with CAD is higher in subgroups of patients with multivessel disease^{10),29)} and in those with old MI and abnormal segmental LV contraction at left ventriculography.^{10),12),29)} Accordingly, we tried to better define the correlation existing between EIVA, on one side, and the severity of coronary artery disease, presence of old transmural MI and extent of LV asynergy on the other. It is evident that the results obtained in this study refer only to the population of patients with CAD as selected by us, i.e. on the basis of both a positive exercise test and positive coronary arteriography, and may not be extrapolated to other subgroups of patients selected in a different way. The incidence of EIVA in our population of patients with CAD (48.7%) is intermediate between that observed in some studies (from 30%²⁹⁾ to 62%³⁰⁾) and is close to that reported by others.^{31)–33)}

In contrast with previous studies,^{10),29)} we did not find a significant correlation between the incidence of EIVA and the number of involved coronary arteries, even though EIVA were more frequent in patients with multivessel CAD than in those with single lesions. The incidence of EIVA in our population of patients with old MI was higher than that observed in some studies,^{29),34)} but smaller than the 70% reported by Poblete et al.³⁰⁾ Our patients with old MI showed a significantly higher frequency of EIVA than did those patients without MI. However other authors did not demonstrate significant differences in EIVA between patients with old MI and patients with angina and no old MI.³⁰⁾ Our results indicate that in our study population, whether subdivided according to the number of coronary stenoses or to the presence of electrocardiographic evidence of old MI, EIVA are more frequent and severe in patients with more advanced degree of LV contraction abnormalities. With an equal degree of coronary arterial narrowing, patients with normal left ventriculography have an incidence of EIVA between 10 and 30%, while those with ASWM have one between 30 and 100%. Patients with or without old MI, if with equal degree of LV contraction impairment, show similar incidence of EIVA (Table III). Thus it is likely that the higher frequency of EIVA in patients with multivessel CAD and old MI reflects a greater impairment of LV wall motion. Diverging results reported in the literature could possibly be related to different composition of study population, in terms of percent of patients with ASWM at left ventriculography.

That the extent of LV asynergy is the major determinant of EIVA is demonstrated by the significant increase in incidence and severity of EIVA in patients with more severe impairment of LV contraction. In fact, most serious arrhythmias occurred in patients with more advanced degrees of asynergy, whereas patients with normal left ventriculography showed a low incidence of EIVA, even if they had multivessel CAD. Our results are in agreement with other studies demonstrating a positive correlation between EIVA and the angiographic severity of CAD.^{10),12)-14),29)} Furthermore, a study conducted with Holter monitoring of the electrocardiogram has shown a positive correlation between the presence and severity of ventricular arrhythmias and hemodynamic and angiographic indices of LV functional impairment, such as a high LV end-diastolic pressure and a wide extent of abnormal LV wall motion.²⁰⁾

We have also observed, even in patients with severe CAD, the disappearance of ventricular arrhythmias during exercise.^{10),13),35)} In agreement with other studies,^{10),12),35),36)} ventricular arrhythmias were more frequently observed in the recovery period, but this was not associated with more severe CAD in comparison to patients with ventricular arrhythmias appearing during exercise. Furthermore, the occurrence of EIVA at heart rates equal to or less than 130 beats/min, as was generally the case in our study, confirms the observations by McHenry et al,¹²⁾ who showed that patients with CAD develop ventricular arrhythmias at lower heart rate than normal subjects showing ventricular ectopy on exercise.^{9),11),12),14)}

We were not able to find any correlation between exercise induced myocardial ischemia, as evaluated by ST segment depression, and EIVA. Such a correlation was demonstrated by Helfant et al,¹³⁾ but not by others.^{10),12),36)} In our study, arrhythmias occurred before ischemic electrocardiographic changes in some patients, while in others they were observed during the recovery period well after the appearance of significant ST segment depression. It has been proposed that EIVA reflect both regional myocardial ischemia and increased sympathetic tone,³⁷⁾ or that EIVA indicate only subclinical myocardial ischemia.¹⁰⁾

In summary, our results show a better correlation between EIVA and the extent of LV asynergy than between EIVA and number of vessels involved, and suggest that EIVA, in this highly selected population, might reflect the severity of LV functional impairment. This could be further supported by the results of the correlations between the extent of LV contraction abnormalities and the hemodynamic indices of LV performance. Left ventricular end-diastolic pressure was significantly higher and cardiac index and LV dP/dt max were significantly lower in patients with more severe LV asy-

nergy. Similar functional stratification was not obtained by subdividing patients by the number of vessels involved.

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