Exercise Testing Early After Myocardial Infarction: Comparison with Echocardiography, Electrocardiographic Monitoring and Coronary Arteriography

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Summary

Background: **Predischarge exercise testing early after myocardial infarction is useful for risk stratification, exercise prescription, and assessment of prognosis and treatment.**

Objective: **The objective of this study was to compare the findings of exercise testing early after myocardial infarction with those of echocardiography, electrocardiographic monitoring (24-hour Holter monitoring) and coronary angiography.**

Methods: **We evaluated 60 cases (mean age of 51.42 ± 9.34 years), of which 46 were males (77%). The symptom-limited maximal exercise test according to the Naughton protocol12 was performed between the sixth day of hospitalization and hospital discharge, with the patients on medication. During hospitalization, the patients underwent echocardiography, electrocardiographic monitoring and coronary angiography.**
The significance level was set at 0.05 (α = 5%).

Results: **Exercise testing had a poor performance in the detection of multivessel coronary artery disease (sensitivity, 42%; specificity, 69%). No significant differences were found when the presence of ischemia on exercise test was compared with multivessel coronary disease, complex ventricular arrhythmias on electrocardiographic monitoring, and the finding of an ejection fraction lower than 60% on echocardiography (p = 0.56), as well as with the presence of multivessel lesions, complex ventricular arrhythmias on electrocardiographic monitoring and abnormal ejection fraction on echocardiography (p = 0.36).**

Conclusion: **The presence of ischemia during exercise testing was associated with the occurrence of ventricular arrhythmias on electrocardiographic monitoring, with reduced ejection fraction on echocardiography, as well as with the presence of multivessel coronary lesions, which constitutes an indicator of a high coronary risk. (Arq Bras Cardiol 2008; 90(3):176-181)**

Key words: **Coronary arteriosclerosis; exercise test; echocardiography; angiography; electrocardiography, ambulatory.**

Introduction

Predischarge exercise testing (ET) early after myocardial infarction (MI) is useful for risk stratification and assessment of prognosis. In ET early after MI, ST-segment depression, angina pectoris, abnormal systolic blood pressure (SBP) response and reduced aerobic capacity are related to adverse outcomes[1-6]. Functional assessment enables treatment evaluation and prescription of work, recreation and rehabilitation activities[7,8]. ET early after myocardial infarction is a safe procedure, with a mortality rate of 0.03% to 0.12%[9,10], morbidity of 0.09%[9], and incidence of subacute stent thrombosis of 0.02%[11].

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The objective of this study was to compare the findings of ET early after MI with those of echocardiography (ECHO), electrocardiographic monitoring (24-hour Holter monitoring) (ECGM), and coronary angiography (CAG).

Methods

This prospective cross-sectional study included a series of consecutive patients of the Coronary Unit of *Hospital São Paulo*. Of the 278 patients admitted with a diagnosis of MI, 60 were evaluated (mean age of 51.42 ± 9.34 years); 46 were males (77%). The organization chart for exclusion of cases is shown in Figure 1.

Diagnosis of MI was confirmed by the presence of two or more of the following criteria: 1) Chest or retrosternal pain, whether constricting or burning; radiating to the upper limbs, neck and back or not, lasting > 30 minutes; and not relieved by vasodilators; 2) ST-segment elevation > 1 mV in ≥2 leads;

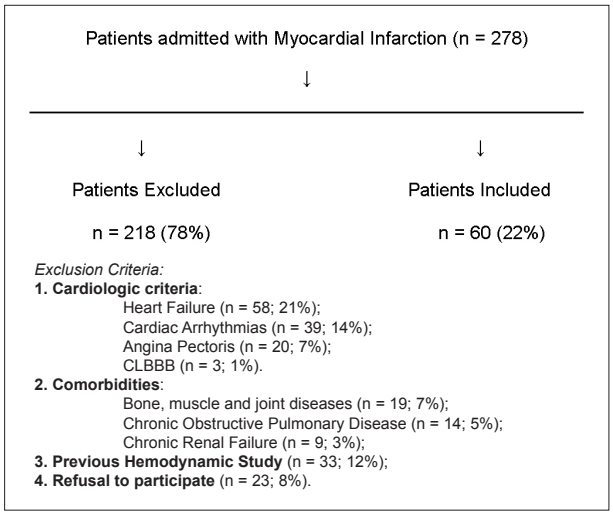

Fig. 1 - Organization chart representing the exclusion criteria.

3) Increased CK-MB and CPK levels, two times the normal values. Patients aged less than 70 years, in New York Heart Association functional class I, with no post-MI angina, complex ventricular arrhythmias or electrocardiographic instability were included. Patients with chest pain in the three preceding days, uncontrolled hypertension, previous revascularization, left ventricular thrombus, walking difficulty, disabling disorders for the performance of ETe and those who refused to participate in the study were excluded.

ECG showed 38 Q-wave MI (63%), 22 non-Q-wave MI (37%), in inferior wall (55%), septal (25%), and lateral wall (3%).

The patients were receiving aspirin (93%), beta blockers (83%), nitrates (76%), angiotensin-converting enzyme inhibitors (60%) and calcium antagonists (15%). Thirty five patients underwent streptokinase thrombolysis (58%).

The study was approved by the Research Ethics Committee of *Universidade Federal de São Paulo – Escola Paulista de Medicina*. A written informed consent was obtained from all patients.

The patients underwent ET, ECHO, ECGM and CAG prior to hospital discharge, on their usual medications.

The symptom-limited maximal exercise test according to the Naughton et al[12] was performed between the sixth day of hospitalization and hospital discharge. The TRACKMASTER TM treadmill (Pensacola, Florida) and the APEX 2000 TEB System (Sao Paulo, Brazil) with 13 leads (12 conventional leads plus CM5) were used. ST-segment alterations ≥ 0.10mV (horizontal, depression) or ≥ 0.20mV (elevation) were considered significant, and ET with significant ST-segment alteration, U-wave inversion and angina were considered ischemic. ET with abnormal ST-segment, U-wave inversion, angina, grade II-IV ventricular arrhythmias (Lown), and abnormal SBP responses (SBP peak < 110 mmHg, SBP increment < 30 mmHg)[8] were considered abnormal. The predicted maximum heart rate was calculated using the Karvonen e cols.[13] formula.

ECHO was performed using parasternal (long and short axes) and apical (four and two-chamber) views, with an Ultramark 4 CV (Bothell, WA) equipment with a 3-MHz transducer. Ejection fraction was calculated using the cube method (reference values: 0.60 to 0.80)[14].

ECGM was recorded in the V1 and CM leads, using a Dynamis 2000 – *Cardios Sistemas* (Sao Paulo, Brazil) equipment and a DMI Cardios model Cardiology 4300 (*Cardios Sistemas*, SP, Brazil) analyzer.

CAG was performed using the Sones technique in the left anterior oblique, right anterior oblique and left lateral views. Obstructions > 70% of the arterial lumen were considered significant[15].

The following tests were used for the statistical analysis: 1) Fisher's exact test for the relationship between the ability to detect ventricular arrythmias on ETe and on ECGM; 2) Cochran test for the concordance between the assessments carried out by ETe, ECHO, ECGM and CAG; 3) Student's t test for the mean endurance time in relation to the CAG, ECHO, abnormal ETe, ischemic ETe and ECGM variables; 4) Pearson's chi square test or Fisher's test for the relationship between the variables and the groups established, considering critical endurance time values those ≤12; 5) Kruskal-Wallis test and ANOVA for comparison of endurance time according to the angiographic lesions. Significance level was set at 0.05 (α = 5%).

Results

Exercise Testing

ETs were performed uneventfully 10.85 ± 3.46 days after MI (Table I). The ST-segment was normal in 19 cases (31%), upsloping in 21 cases (35%), horizontal in 16 cases (27%), downsloping in 4 cases (7%), and was considered ischemic in 21 patients (35%): 4 upsloping, 13 horizontal and 4 downsloping. No U-wave inversion was observed. Isolated supraventricular extrasystoles were found in five ETe (8%). Ventricular arrhythmias were recorded in six cases (10%): Lown grade II (4 cases), grade III (one case), and grade IV-A (one case). Angina pectoris was present in five patients. In 20 cases, the SBP increment was < 30 mmHg, and in three cases SBP peak was < 110 mmHg.

Echocardiography

Echocardiography recorded enlarged left atrium in six patients (10%) and enlarged left ventricle in nine (15%). Reduced fractional shortening was observed in 23 cases (38%), and reduced ejection fraction in 16 cases (27%). Left ventricular segmental motion was abnormal in 56 patients (93%) with hypokinesia in 21 cases (35%), akinesia in 11 cases (18%) and hypokinesia associated with akinesia in 24 cases (40%). Heart valve disease, pericardial diseases and pulmonary hypertension were not detected.

Electrocardiographic Monitoring

Electrocardiographic monitoring showed sinus rhythm in all cases (Table I). Angina was not recorded. Supraventricular arrhythmias occurred in 58 patients (96%): isolated extrasystoles in 58 (96%), paired extrasystoles in 12 (20%),

Table 1 - Exercise test and electrocardiographic monitoring variables.

Variable	Mean ± SD	Median
HRPEAK (bpm)	116 ± 20	112
HRPEAK / HRPREDICTED MAX (%)	67 ± 11	67
SBPREST (mmHg)	114 ± 18	110
SBPPEAK (mmHg)	149 ± 30	148
DPPEAK (mmHg.bpm.10-2)	173 ± 46	176
Δt (days)	11 ± 3	10
HR MIN – ECGM	53 ± 8	54
HR MEAN – ECGM	71 ± 11	72
HR MAX - ECGM	106 ± 20	101

*ECGM – Electrocardiographic monitoring (24-hour Holter System); SD – Standard deviation; HRPEAK – Peak heart rate; HRPREDICTED MAX – Predicted maximum heart rate; SBP – Systolic blood pressure; DP – Double product; **Δt – Time interval** between MI and ETE; HRMIN – Minimum heart rate; HRMEAN – Mean heart rate; HRMAX – Maximum heart rate.*

paroxysmal tachycardia in 9 (15%). Ventricular arrhythmias were recorded in 52 patients (87%): isolated (52 cases, 87%), paired (15 cases, 25%), and in clusters (11 cases, 18%). No sustained ventricular tachycardia or ventricular fibrillation occurred.

Hemodynamic Study

In the hemodynamic study, critical one-vessel lesions were recorded in 27 patients (45%), and multivessel lesions in 24 patients (40%): 1) Left main coronary artery, 1 case (mild); 2) Anterior descending artery, 32 cases (53%), critical in 25 cases (78%); 3) Right coronary artery in 28 patients (47%), critical in 20 cases (71%); 4) Circumflex artery in 23 patients (38%), critical in 16 cases (70%).

The left ventricle was normal in 30 cases (50%), showed a mild dysfunction in 15 cases (25%), was moderate in 12 cases (20%), and severe in two cases (3%).

Relationships between the results of the procedures

The relationship between the results obtained in ET, ECGM and CAG are shown in Tables 2, 3, 4, 5 and 6. No relationship was observed between the presence of ventricular arrhythmias on ET and on ECGM (Table 2); the occurrence of both was independent (p = 0.65%). No difference was found in the number of ventricular extrasystoles on the ECGM of patients with or without ventricular extrasystoles on ET (1298 ± 80, median = 262 vs. 88 ± 325, median = 6, p = 0.23).

No significant associations were found between: 1) The number of ventricular extrasystoles on ECGM and ejection fraction (r = 0.04); 2) The number of ventricular extrasystoles on ECGM and SBP increment (r = -0.16); 3) Ejection fraction and SBP increment (r = 0.10).

ET had a poor performance in the detection of multivessel coronary disease (Table 3).

No significant differences were observed when the presence of ischemia on ET was compared with multivessel coronary disease on CAG, complex ventricular arrhythmias on ECGM, and the occurrence of ejection fraction lower than 60% on ECHO (p = 0.56), as well as with the presence of multivessel lesions on CAG, complex ventricular arrhythmias on ECGM and abnormal ejection fraction on ECHO (p = 0.36) (Table 4).

The endurance time was 16.1 ± 4.7 minutes, ranging from 6 to 21 minutes. It was higher than 12 minutes in 45 patients (75%) and ≥15 minutes in 37 cases (62%), and was compared to the following variables: 1) CAG, as to the presence or absence of critical lesions; 2) ECHO, as to an ejection fraction lower than or higher than 60%; 3) Abnormal ET, as to the presence or absence of abnormalities; 4) Ischemic ET, as to the presence or absence of ischemia; 5) ECGM, as to the presence or absence of complex ventricular arrhythmias. Only the differences for abnormal and ischemic ET (p = 0.07 and p = 0.08, respectively) showed a trend to significance (Table 5). Endurance time values equal to or higher than 12 or 15 minutes bore no relation to the occurrence of severe coronary lesions on CAG, of ejection fraction lower than 60% on ECHO, and of ischemic ST-segment on ET. However, they were significant in relation to the occurrence of abnormal ET (Table 6).

Discussion

Predischarge ET early after MI is recommended in the following situations: 1) Class I, for prognostic assessment, physical activity prescription and evaluation of therapy; 2) Class IIb, for detection of myocardial ischemia after CAG, in cases in which the coronary lesions cannot be evaluated; 3) Class IIb, in patients with ECG changes that can interfere with the analysis of the ST-segment; 4) Class III, in cases with comorbidities that limit life expectancy or myocardial revascularization[16].

Table 2 - Incidence of ventricular arrhythmias and complex ventricular arrhythmias on exercise test and on electrocardiographic monitoring (24-hour Holter system).

	Group AV		Group CAV		
Variable	n	%	n	%	Comparative test
ET	4	14.29	1	5.26	p=0.655
ECGM	34	85.71	18	94.74	

AV - ventricular arrhythmias; CAV - complex ventricular arrhythmias; ET - exercise test; ECGM - electrocardiographic monitoring (24-hour Holter system).

Despite the symptom-limited protocol, our findings showed a maximum heart rate of 116 ± 20 bpm, corresponding to 66.9 ± 11.2% of the predicted maximum rate, thus complying with the established guidelines[16]. These values were higher than those obtained on ECGM. ET early after MI may be performed using the Bruce protocol within three days of hospital admission with a low incidence of complications. In symptom-limited ET early after MI the maximum heart rate reached was 116 ±1bpm (72.2 ± 0.8% of the predicted maximum)[17].

SBP showed, on average, an increment from 114 ± 18mmHg to 149 ± 30mmHg. This increment was abnormal in 33% of the cases. This has been attributed to ischemic ventricular dysfunction, physical deconditioning, and use of beta-blockers, as well as to left ventricular baroceptor alterations[8].

Table 3 - Performance of the exercise test on coronary artery disease.

Variable	ACD (%)	MV-ACD (%)
Sensitivity	37	42
Specificity	78	69
Positive predictive value	90	48
Negative predictive value	18	64
Efficacy	43	58

ACD - Atherosclerotic coronary disease; MV-CAD - Multivessel ACD.

The double product provides an estimate of myocardial oxygen consumption[7]. Reference values correspond to levels ≥ 25000bpm.mmHg[8,18]. Our patients reached 17335 ± 4654bpm.mmHg, probably due to factors that influenced the heart rate and blood pressure, especially the use of beta-blockers[11]. In general, despite the regional contractility alterations, the patients had, preserved ventricular function, with reduction of fractional shortening by 38%, of ejection fraction by 27%, and of the prevalence of abnormal ventriculography of moderate and severe degrees by 23%. The use of the planar method for the calculation of ejection fraction would have provided more reliable results.

The ability of ET early after MI in the detection of multivessel coronary disease showed a sensitivity and specificity of 58% and 82%, respectively, for ST-segment alterations, and 40% and 83% for the occurrence of angina during ET[9]. Our findings are similar, showing a poor performance of ET early after MI, with an accuracy of 58%. These results were facilitated by the use of drugs, by the test protocol, and by the occurrence of MI in the anterior wall. A significant reduction of ET sensitivity was demonstrated in patients with pathological Q waves from V1 to V4[19].

The occurrence of cardiac arrhythmias on ET early after MI has been related to myocardial ischemia and ventricular dysfunction[20,21]. Patients with ventricular arrhythmias have a high prevalence of infarct-related artery stenosis, peri-infarction ischemia and ischemia in multivessel distribution[21]. In this study, ventricular arrhythmias were more frequently

Table 4 - Variables used in the comparison of endurance time.

Variable	Positive Category	Negative Category
Coronary angiography	Severe ACD	No severe ACD
Echocardiography	EF < 60%	EF > 60%
Abnormal Exercise Test	Abnormality during exercise testing	No abnormality during exercise testing
Ischemic Exercise Test	Ischemia during exercise testing	No ischemia during exercise testingo
Electrocardiographic Monitoring (24-hour Holter)	Complex ventricular arrhythmia	No complex ventricular arrhythmia

ACD - atherosclerotic coronary disease; EF - ejection fraction.

Table 5 - Endurance time values in relation to coronary angiography. echocardiography. electrocardiographic monitoring and ischemic and abnormal exercise test variables.

Variable	Category	Mean	SD	Median	n	t test
CAG	+	14.8	4.8	15.1	24	p=0.1
	-	16.9	4.5	18.4	36	
ECHO	+	16.4	3.7	16.0	16	p=0.8
	-	16.0	5.0	17.2	40	
IET	+	14.7	5.3	15.2	21	p=0.09
	-	16.8	4.2	17.8	39	
AET	+	15.1	5.0	15.1	32	p=0.08
	-	17.2	4.0	17.9	28	
ECGM	+	16.0	5.1	17	19	p=0.10
	-	16.1	4.5	16.8	41	

CAG – Coronary angiography (+. with critical lesions); ECHO – Echocardiography (+. with abnormal ejection fraction); IET – Ischemic exercise test (+. with ischemic ST-segment. U-wave inversion and/or angina); AET – Abnormal exercise test (+. with ischemia. ventricular arrhythmia and/or abnormal SBP response); ECGM – Electrocardiographic monitoring (24-hour Holter System) (+. with complex ventricular arrhythmia); SD – Standard deviation.

Table 6 - **Distribution of frequency of coronary angiography. echocardiography. abnormal exercise test. ischemic exercise test and electrocardiographic monitoring variables for the groups with endurance time ≤ 12 minutes and > 12 minutes. and for the groups with endurance time ≤ 15 minutes and > 15 minutes.**

Variable	C	Group				CT	Group				TC
		≤ 12 minutes		> 12 minutes			≤ 15 minutes		> 15 minutes		
		n	%	n	%		n	%	n	%	
CAG	+	8	53.33	16	35.56	p=0.224	12	52.17	12	32.43	p=0.129
	-	7	46.67	29	64.44		11	47.83	25	67.57	
ECHO	+	3	21.43	13	30.95	p=0.495	6	27.27	10	29.41	p=0.863
	-	11	78.57	29	69.05		16	72.73	24	70.59	
AET	+	11	73.33	21	46.67	p=0.073	16	69.57	16	43.24	p=0.047*
	-	4	26.67	24	64.44		7	30.43	21	56.76	
IET	+	7	46.67	14	31.11	p=0.274	10	43.48	11	29.73	p=0.278
	-	8	64.44	31	68.89		13	56.52	26	70.27	
ECGM	+	7	46.67	12	26.67	p=0.202	7	30.43	12	32.43	p=0.875
	-	8	64.44	33	73.33		16	69.57	25	67.57	

C - Category; CT - comparative test; CAG - coronary angiography; ECHO - echocardiography; AET - abnormal exercise test; IET - ischemic exercise test; ECGM - electrocardiographic monitoring (24-hour Holter System).

observed on ECGM. There was no relation between the occurrence of arrhythmias on ET and on ECGM. The degree of ventricular extrasystoles on ECGM did not show any correlation with ejection fraction and SBP increment. The sample size may have interfered with these results.

However, no significant differences were found between the procedures, considering ET with myocardial ischemia, ECHO with reduced ejection fraction, ECGM with complex arrhythmias, and CAG with multivessel lesions. These procedures had the same value in the identification of cases presenting with alterations.

Inability to reach a 5-MET workload during ET early after MI is related to adverse outcomes[7]. Patients able to reach 5 to 6 METs had a mortality of 1 to 2% in the first year[1]. Functional capacity is a strong predictor of death and reinfarction, irrespective of treatment strategy; the prognostic value of ST-segment depression is more evident in fibrinolysis-treated patients[20].

Endurance time enables the estimation of the aerobic capacity[7] and is considered predictive of post-infarction coronary events[2,5,6,7,22]. Inability to complete six minutes of exercise was predictive of mortality[5]. In this study, we used the Naughton protocol, in which the 5-MET workload would correspond to a 12-minute endurance time. No significant differences were found in endurance time in relation to the presence of ischemia on ET, reduced ejection fraction on ECHO, complex ventricular arrhythmia on ECGM and multivessel lesions. Patients with ischemic or abnormal ET showed a non-significant trend to lower values of endurance time. The analysis of these results was affected by the sample size.

In general, our results were influenced by the inclusion criteria, which led to an interpretation bias because patients with a favorable clinical outcome, occasionally favorable prognosis and receiving medication were selected. Repetitive ventricular arrhythmias and ST-segment changes are more frequent in patients off pharmacological therapy. Drug discontinuation is well tolerated soon after MI; however, there is a risk that must be taken into account as a criterion of drug discontinuation[23].

Patients unable to undergo ET early after MI had a higher mortality in Froelicher et al[1] meta-analysis (1987), in the pre-thrombolytic era[1], and in GISSI-2 and TIMI-2 trials, as well as in Arnold et al[4] findings (1993), in the thrombolytic era[3,6].

The limitations of the present study were: 1) The conclusions are valid in cases of non-complicated MI; 2) Sample size.

Conclusions

In this study, exercise testing early after myocardial infarction showed a low value in the detection of multivessel coronary artery disease. However, the presence of ischemia during the test was associated with the occurrence of ventricular arrhythmias on ECGM, with reduced ejection fraction on ECHO, and with the presence of multivessel coronary lesions, which constitutes an indicator of a high coronary risk.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Study Association

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