Cardiac Rehabilitation in Patients With Myocardial Infarction: a 10-Year Follow-up Study

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Introduction and objectives. Very little information is available on the effect of cardiac rehabilitation programs on long-term survival. The primary aim of this study was to assess the effect of a structured cardiac rehabilitation program on mortality in patients who had suffered acute myocardial infarction. The secondary endpoint was the effect on morbidity.

Patients and method. The study included 180 low-risk male patients aged under 65 years. Patients were randomly assigned to one of 2 groups: 90 entered into a comprehensive cardiac rehabilitation program, and 90 served as a control group. The mean follow-up period was 10 years.

Results. All-cause mortality was significantly lower in the intervention group: the 10-year survival rate was 91.8% in the intervention group compared with 81.7% in the control group (*P*=.04). There was also a decrease in cardiovascular mortality, though it was not statistically significant: the 10-year survival rate was 91.8% in the intervention group compared with 83.8% in the control group (*P*=.10). The incidence of non-fatal complications was lower in the intervention group (35.2% vs 63.2%, *P*=.03), as was the incidence of unstable angina (15.7% vs 33.9%, *P* =.02) and cardiac heart failure (3.0% vs 14.4%, *P*=.02), and the need for coronary intervention (8.4% vs 22.9%, *P*=.02).

Conclusions. The application of a comprehensive cardiac rehabilitation program significantly decreased long-term mortality and morbidity in low-risk patients after acute myocardial infarction.

Key words: *Myocardial infarction. Survival. Secondary prevention. Cardiac rehabilitation. Mortality.*

Rehabilitación cardíaca en pacientes con infarto de miocardio. Resultados tras 10 años de seguimiento

Introducción y objetivos. Hay muy pocos estudios en los que se analicen los resultados de los programas de rehabilitación cardíaca sobre la supervivencia a largo plazo. El objetivo fundamental del presente trabajo es analizar la mortalidad y el secundario, la morbilidad, en pacientes que realizan estos programas después de haber presentado un episodio de infarto de miocardio.

Pacientes y método. Se incluyó a 180 pacientes varones, con edad < 65 años y criterios de bajo riesgo. Se dividieron de forma aleatoria en 2 grupos: el primero de ellos (90 pacientes) realizó un programa de rehabilitación; los 90 restantes formaron el grupo control. La mediana de seguimiento fue 10 años.

Resultados. Hubo un descenso significativo en la mortalidad por todas las causas (supervivencia a los 10 años del 81,7% en el grupo control y del 91,8% en el grupo de intervención; p = 0,04); la mortalidad por causa cardiovascular también descendió, aunque de forma estadísticamente no significativa (supervivencia a 10 años del 83,8% en el grupo control y del 91,8% en el grupo de intervención; p = 0,10). El porcentaje de pacientes con complicaciones no mortales fue inferior en el grupo de actuación (el 35,2 frente al 63,2%; p = 0,03) y tuvieron significación estadística el descenso en la presentación de angina inestable (el 15,7 frente al 33,9%; p = 0,02), insuficiencia cardíaca (el 3,0 frente al 14,4%; p = 0,02) y la necesidad de cirugía de revascularización (el 8,4 frente al 22,9%; p = 0,02).

Conclusiones. La rehabilitación cardíaca en pacientes de bajo riesgo tras un infarto agudo de miocardio da lugar a descensos significativos en la mortalidad y en la incidencia de nuevos eventos a largo plazo.

Palabras clave: *Infarto de miocardio. Supervivencia. Prevención secundaria. Rehabilitación cardíaca. Mortalidad.*

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INTRODUCCION

The application of cardiac rehabilitation programs (CRP) following acute myocardial infarction (AMI)

ABBREVIATIONS

CV: cardiovascular.
CG: control group.
RG: rehabilitation group.
AMI: acute myocardial infarction.
CRP: cardiac rehabilitation program.

has demonstrated their efficacy in increasing functional capacity,[1-3] controlling coronary risk factors,[2,4-6] reducing symptoms,[7] and countering psychological deterioration.[8,9] They have also been shown to improve cost-efficiency.[10,11]

Given that ischemic heart disease is a progressive, chronic illness and that low-risk patients are included in CRP, possible beneficial effects of these therapeutic programs on morbidity and mortality require long-term evaluation.

The present study was designed to compare the clinical evolution of 2 groups of patients with AMI: one following our multidisciplinary CRP and the other receiving conventional treatment.

Our principal objective was to analyze and compare incidence of death in both groups at 10-year follow-up; the secondary objective was to analyze complications occurring in the same period.

PATIENTS AND METHOD

Selection of Patients

We enrolled 180 consecutive male patients diagnosed with AMI and admitted to the coronary care unit of our hospital. Enrolments were based on the American Association of Cardiovascular and Pulmonary Rehabilitation inclusion criteria[12]: age <65 years, low-risk (hospital course without complications, absence of signs of myocardial ischemia, functional capacity >7 metabolic equivalent time [MET], ejection fraction >50%, and absence of severe ventricular arrhythmias).

Patients were excluded on grounds of age and gender because of evidence that very few women are found with infarction and in an age range lower than that described. We set the age limit at 65 years, retirement age, because a high percentage of older patients abandon CRP for a variety of reasons.

All patients gave signed informed consent according to unit procedure and the study was approved by our hospital ethics committee.

The 180 patients were randomized into 2 groups: one followed our cardiac rehabilitation program (RG) and the other, the control group (CG), received conventional treatment and served as a point of reference.

The Hospital Ramón y Cajal CRP[13] begins at 2 weeks post- discharge and consists of:

1. Three months supervised, individualized physical training.
2. Psychological program including behavior modification techniques, group therapy, and relaxation sessions.
3. Educational program on modifying lifestyle and controlling coronary risk factors.
4. Return to work counseling.

Physical training consisted of 3 1-hour sessions per week in the hospital gym. At each session, patients followed a table of physiotherapy and aerobic training on mats or an exercise bicycle.

During training, heart rate was calculated individually following stress exercise treadmill tests (Bruce protocol) at the start and end of the program. The initial test served to filter enrolments and patients with ischemia and low exercise levels were excluded and indicated for coronary angiography.

Patients with exercise tests without signs of ischemia had their target heart rate set at 75% of the maximum achieved for the first 6 weeks of training and 85% for the last 6 weeks.

Supervised training was complemented by progressively increasing daily walks of ≤1 hour in duration, when patients tried to maintain the heart rate achieved during training. Walks were undertaken by patients individually and were unsupervised.

The psychological program consisted of individualized evaluation of psychological profile using tests to evaluate anxiety (Hamilton),[14] depression (Zung),[15] and personality (Bortner),[16] and Schultz method relaxation techniques[17] practiced 2 days per week. Once a week patients underwent group therapy. Patients with greater deterioration received individualized treatment from psychologists and, if needed, from the unit psychiatrist.

The educational program involved a weekly seminar for patients and immediate family to inform and advise about the illness and the need to modify coronary risk factors and lifestyle.

Return to work counseling included social and vocational evaluation and recommendations on post-discharge return to work.

Phase II CRP interventions were performed full- or part- time by staff of a multidisciplinary unit depending on the cardiology service and consisting of 4 cardiologists, 1 rehabilitation specialist, 2 psychologists, 1 psychiatrist, 2 nurses, 2 physiotherapists, and 1 social worker.

Phase III of the program covered the rest of the patient's life. According to the discharge report, patients continued to take physical exercise 4-5 days a week, followed relaxation guidelines 2-3 times per day, and controlled risk factors. For 4 years, patients attended

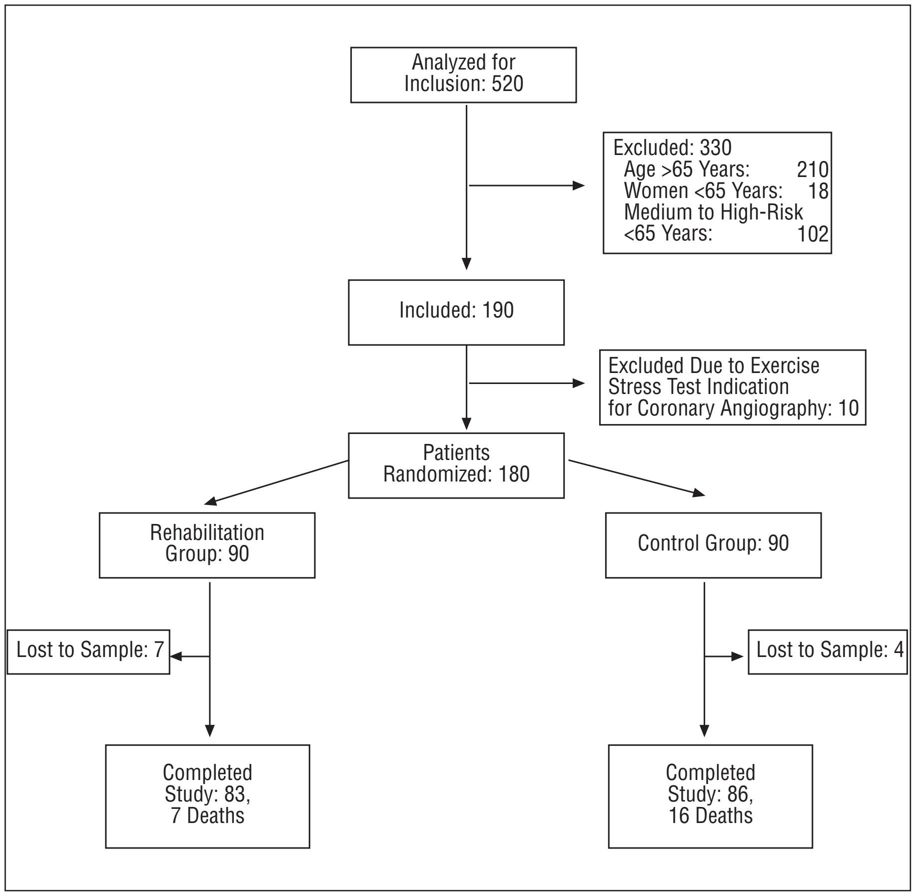

Figure 1. Flow chart of the study with randomization of patients admitted for acute myocardial infarction.

the hospital rehabilitation unit once a month for physical training and relaxation sessions to support them in fulfilling CRP recommendations.

Following current unit norms, patients were later advised to continue taking exercise individually or in a gym following specific training norms in the discharge report.

After post-AMI discharge, CG patients were advised to take standard secondary prevention measures: stop smoking, follow a low cholesterol diet, and take physical exercise, without following a structured CRP.

Patients in both groups underwent periodic cardiologic outpatient clinic check-ups at 1, 3, 6, and 12 months during the first year, and once a year or according to need thereafter, up to the time of writing.

To avoid differences in clinical management during follow-up, all patients were reviewed and treated by the 4 rehabilitation unit cardiologists. Medical treatment during follow-up was that considered adequate by the cardiologists responsible for clinical control of the patients.

Statistical Analysis

Chi-squared was used to compare percentages. In both groups, we calculated Kaplan-Meier survival curves and compared these using log-rank tests. Values of $P<.05$ were considered statistically significant.

RESULTS

During the 2-year enrolment period, 520 patients with AMI were admitted to the hospital coronary unit. We excluded those who did not fulfill the previously described criteria (n=330). After initial exercise tests, 10 patients were excluded with indication for coronary angiography due to signs of ischemia at low load levels.

The remaining 180 were randomized into 2 groups of 90: 1 group (RG) followed the CRP and the other (CG) served as a reference.

At 10-year check-up, 11 patients had been lost (7 RG and 4 CG), leaving 83 and 86 patients, respectively (Figure 1).

Baseline patient characteristics were similar in both groups (Table 1). Medical treatment at discharge did not show differences.

At 10-year follow-up, all-cause mortality was 7 RG patients (7.7%) and 16 CG patients (17.7%) with survival curves showing statistically significant differences (P=.04) of 91.8% and 81.7%, respectively (Figure 2).

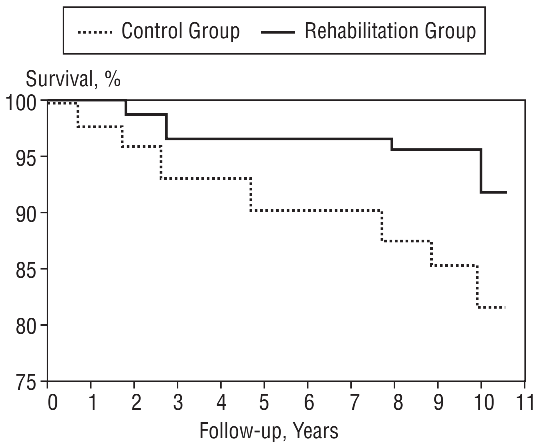

Figure 2. Ten-year mortality (Kaplan-Meier curves). We found a significant reduction in mortality in the rehabilitation group.

All RG patient deaths were due to cardiovascular (CV) causes, making CV mortality the same as all-cause mortality (7.7%). Two CG patients died of non-CV causes (1 cirrhosis and 1 neoplasia) with 15.5% CV mortality. At 10 years, CG survival was 83.8% and RG survival was 91.8% (*P*=.10).

Specific causes of mortality in each group appear in Tables 2 and 3. Mortality due to sudden death was 2.2% (RG) and 4.4% (CG) (*P*=.68). Secondary mortality due to reinfarction was 4.4% (RG) and 4.4% (CG) and that due to heart failure was 1.1% (RG) and 4.4% (CG) (*P*=.37).

During the mean 10-year follow-up, the proportion of patients with non-fatal complications was higher in the CG (63.2%) than in the RG (35.2%) (*P*=.03).

Data on the etiology of complications are in Table 4. Percentages refer to the number of patients for whom we had information on each variable. We found a significant fall in unstable angina (*P*=.02), heart failure (*P*=.02), and need for revascularization surgery (*P*=.02). Non-fatal reinfarction and need for coronary angioplasty were also less frequent but not statistically significant (*P*=.40 and *P*=.50, respectively).

TABLE 1. **Baseline Characteristics of Patients***

	Control Group	Rehabilitation Group
Age, mean±SD	52.6±9	50.3±6
Previous AMI	1.1%	4.8%
Diabetes	8.9%	6.0%
AHT	22.7%	24.4%
Dyslipidemia	22.1%	28.1%
Smoking	86.2%	95.2%
Site of AMI		
Anterior	48.3%	40.0%
Inferior/posterior	46.3%	48.3%
Non-Q wave	5.3%	11.6%

*SD indicates standard deviation; AHT, arterial hypertension; AMI, acute myocardial infarction.

TABLE 2. **Characteristics of Rehabilitation Group Patients Who Died***

No. Order	Initial Age, Years	AMI Site	Cause of Death	Years Survival
11	63	INF-POS	Sudden death	10
18	39	INF	Re-AMI	8
24	64	INF	Re-AMI	2
33	57	INF	Re-AMI	2
38	65	ANT	APE	10
47	58	ANT	Re-AMI	3
56	59	ANT	Sudden death	10

*ANT indicates anterior; APE, acute pulmonary edema; AMI, acute myocardial infarction; INF, inferior; POS, posterior.

TABLE 3. **Control Group Patients Who Died***

No. Order	Initial Age, Years	AMI Site	Cause of Death	Years Survival
6	57	ANT	Sudden death	10
8	51	ANT	Re-AMI	5
21	56	ANT	Sudden death	8
28	56	INF	Cancer	8
32	61	ANT-LAT	Sudden death	9
37	49	INF	ACVA	10
42	48	ANT-LAT	Re-AMI	2
51	62	INF	HF	5
59	62	INF	APE	10
60	65	INF	ACVA	3
62	53	Septal	Sudden death	4
64	62	ANT	Cirrhosis	2
69	50	ANT	APE	2
73	58	Non-Q wave	Re-AMI	1
78	55	ANT	HF	9
89	59	INF	Re-AMI	1

*ACVA indicates acute cerebrovascular accident; ANT, anterior; APE, acute pulmonary edema; AMI, acute myocardial infarction; HF, heart failure; INF, inferior; LAT, lateral; POS, posterior.

DISCUSSION

Results of this long-term follow-up, randomized study of patients at low-risk of infarction show that cardiac rehabilitation programs significantly reduce mortality and percentage of complications, especially revascularization, unstable angina, and heart failure.

Modification of lifestyle behaviors such as smoking, eating abundant quantities of fats, sedentary habits, and methods of dealing with stress, can significantly reduce risk of coronary heart disease. Similarly, better fulfillment of therapeutic guidelines to treat hypertension, diabetes and dyslipidemia can prevent the ap-

TABLE 4. **Morbidity***

	Control Group	Rehabilitation Group	*P*
Unstable angina	33.9%	15.7%	.02
Reinfarctions	14.8%	9.7%	.40
Heart failure	14.4%	3.0%	.02
Heart surgery	23.0%	8.5%	.02
PTCA	10.2%	5.6%	.0

*PTCA indicates percutaneous transluminal coronary angioplasty.

pearance or progression of atherosclerosis. According to some estimates, >50% of the reduction in mortality due to coronary artery disease is attributable to behavior changes.[18]

Multidisciplinary CRP in coronary patients is aimed at modifying risk profiles through the acquisition of heart-healthy habits and lifestyles.

Studies that analyze the effects of CRP on morbidity and mortality are inconclusive. This may be explained by the reduced number of patients enrolled and the fact that these are low-risk patients with low annual mortality.

Long-term follow-up studies entail risks of sample erosion, intervention cross-sectional and the appearance of new therapies. We believe we have avoided many of these through regular check-ups by Unit cardiologists and guidelines drawn from similar interventions. For example, medication regimens employed in secondary prevention (beta-blockers, angiotensin converting enzyme inhibitor and antiplatelet drugs) at discharge were clearly insufficient by standard criteria but currently meet Spanish and European guidelines.

Several meta-analyses have studied mortality in randomized trials producing inconclusive results.[19-22] The last and perhaps the most thorough of these included 48 studies and 8940 patients and found a fall in all-cause and CV mortality.[22]

These explanations may justify the fact there are only 2 publications on long-term CRP results. In Finland, Hämäläinen et al[23,24] followed the evolution of 375 patients, 188 on a CRP and 187 serving as a control group. They found a significant reduction in sudden death and all-cause coronary death at 10 and 15 years in the intervention group.

In Sweden, in 1987 and 1993, Hedbäck et al[25,26] published at 5- and 10-year results of a prospective, non-randomized study including patients from 2 hospitals drawing on the same geographic area and social environment. Patients from 1 hospital (n=147) underwent cardiac rehabilitation and those from the other (n=158) served as a control group. Only 84 intervention group patients undertook physical training. At 5 years, the authors found no differences in mortality but at 10 years they detected reductions in all-cause and CV mortality in the intervention group.

In our study, 10-year all-cause mortality in the RG was reduced by 56.5%. Note that mortality was low in both groups (7.7%, RG; 17.7%, CG) by comparison with the earlier studies. Hämäläinen et al[23] reported 10-year all-cause mortality of 43.6% in the RG and 51.9% in the CG; Hedbäck et al[26] reported 42.2% in the RG and 57.6% in the CG.

These differences could be explained in several ways: *a)* the natural history of ischemic heart disease in Spain differs from that of other countries, with a lower rate of post-IAM mortality[27]; *b)* our sample, selected on inclusion criteria, consisted of low-risk patients; *c)* the mean age of our patients (51 years) was lower than that of the other studies (Hämäläinen et al,[23] 54 years; Hedbäck et al,[26] 57 years), perhaps meaning a better prognosis[27]; and *d)* our patients were enrolled 10 years after the other 2 studies and clinical management and treatment would have improved.

Since year 1 of follow-up, we found more deaths in the CG than in the RG and this pattern has been maintained throughout the study. At 4 and 6 years differences were not statistically significant, perhaps due to low mortality rates.[28,29] However, at 10 years, the greater number of deaths led to statistically significant differences.

Belardinelli et al[30] confirmed that low-risk conditions produce significant short-term results. They enrolled 94 patients (mean age 59±14 years) with controlled heart failure randomized into 2 groups. They found that patients following a CRP (n=48) had a significant reduction in mortality (*P*=.01) versus control group patients (n=46) after a mean 14-month follow-up.

Most deaths in our study patients were due to CV causes. Although the difference between groups was 50.4%, this was not statistically significant, probably due to the limited number of deaths and patients.

As with all-cause mortality, we found markedly lower percentages of CV mortality than those reported by Hämäläinen et al[23] (35.1%, RG; 47.1%, CG) and Hedbäck et al[26] (38.7%, RG; 53.1%, CG), probably for the same reasons.

Our 10-year follow-up results for morbidity showed a 63.15% incidence of CG patients with non-fatal complications, which was much higher than that of the RG (35.15%) and statistically significant (*P*=.03).

As in other follow-up studies and the meta-analysis,[19-22] we found no significant differences in the number of non-fatal reinfarctions. However, there was greater incidence of unstable angina (*P*=.02) leading to admission and explaining the greater need for surgery among CG patients. The low incidence of angioplasty was related to the period when patients were enrolled, when the technique was less well-developed in Spain.

A reduced number of patients presented heart failure in both groups although the incidence of this complication was greater and statistically significant in the

CG (*P*=.02). This was probably due to the positive effect of risk factor control and taking exercise (improved ventricular function, endothelial dysfunction, collateral circulation, etc) widely described in CRP manuals[31].

We should explain why we did not correlate morbidity and mortality results with the parameters of prognostic interest that the CRP aims to control (sedentary habits, psychological deterioration and control of risk factors).

There can be no doubt as to the positive effect of cardiac rehabilitation in these contexts in short-term studies, as Taylor et al's meta-analysis corroborates[22]. However, it is very difficult to show that continuous adherence to advice is maintained in the long-term. The patients in the groups compared may have been crossed and treatment and complete control of risk factors may have varied during their evolution.

Table 1 shows a lower mean age in the rehabilitation group (better prognosis) but the proportion of RG patients with risk factors is clearly greater than that of CG patients. We believe that these data are a consequence of the randomization and number of patients and they do not influence the final results.

However, we think the benefit of CRP is due to the healthy lifestyle habits that patients "learn" while following the program (giving up smoking, changes in diet, taking regular exercise) and that, if this is maintained during the first year post-AMI,[2,8] they are likely to be maintained in the long-term. It would be interesting to continue with "refresher" sessions on a continuous basis, taking advantage of the excellent health service infrastructure available in Spain. However, experience has shown that, for a variety of reasons, this "excellent infrastructure" is totally inefficient at managing this type of intervention.[32]

Finally, we consider our data are of interest because they show results in Spain where incidence of ischemic heart disease is clearly lower than in northern Europe, and because the percentage of patients included in Spanish CRPs is remarkably low, some 3% according to current reports.[33,34]

CONCLUSION

The results of our study support the hypothesis that a multifactor CRP with secondary prevention measures maintained in the long-term favorably influences prognosis in post-AMI patients.

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