Intervention Program to Improve Secondary Prevention of Myocardial Infarction. Results of the PRESENTE (Early Secondary Prevention) Study

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Introduction and objectives. Secondary prevention measures for myocardial infarction are inadequate. In Spain, the earlier PREVESE studies provided preliminary data. The aim of this study was to document the results of a simple intervention program for secondary prevention, implemented during the hospital stay.

Patients and methods. We included 4174 patients (mean age 63.7 years, 73% men) discharged from 110 hospitals after myocardial infarction. Lipid profile was determined during the first 24 h after admission, and before discharge patients and relatives were informed about the disease and its prevention, and were given printed informative materials. The patients were seen again 6 months later.

Results. After 6 months, 82.9% of the patients were examined and 10% were lost to follow-up. Mean blood pressure, weight and body mass index of the sample were lower, and lifestyle variables had improved. At discharge 87% were prescribed statins, 59.4% beta blockers, 51.2% ACE inhibitors and angiotensin blockers, and 94.1% antiplatelet drugs. These prescriptions were still being used 6 months later. There were substantial improvements in lipid values.

Conclusions. The implementation of a simple intervention program for patients with myocardial infarction and their relatives, and the determination of lipid levels within 24 hours of admission, improved the secondary prevention measures at discharge and during the 6-month follow-up period. Acceptance of the program among the patients was good.

Key words: *Myocardial infarction. Prevention. Drugs.*

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Programa de intervención para mejorar la prevención secundaria del infarto de miocardio. Resultados del estudio PRESENTE (PREvención SEcuNdaria TEmprana)

Introducción y objetivos. La prevención secundaria del infarto de miocardio no se realiza de forma adecuada. En España, los estudios PREVESE aportaron datos sobre este problema. El objetivo de este estudio ha sido comprobar el efecto de un sencillo programa de intervención realizado durante la estancia hospitalaria.

Pacientes y método. Se ha incluido, al alta hospitalaria, a un total de 4.174 pacientes postinfarto de 110 hospitales, con una edad media de 63,7 años y un 73% de varones, a los que se ha determinado un perfil lipídico en las primeras 24 h del ingreso y se ha realizado una entrevista informativa, acompañados de sus familiares, con entrega de material educativo; posteriormente fueron revisados a los 6 meses.

Resultados. A los 6 meses se revisó al 82,9% de los pacientes y el 10% no pudo ser localizado. Se observó una mejoría de la presión arterial, el peso y el índice de masa corporal medios de la muestra, así como de los estilos de vida. Al alta hospitalaria, el 87% recibió tratamiento con estatinas, el 59,4% con bloqueadores beta, el 51,8% con inhibidores o bloqueadores de la angiotensina y el 94,1% con antiagregantes plaquetarios, prescripciones que se mantuvieron a los 6 meses. Los valores lipídicos mejoraron sustancialmente.

Conclusiones. Con la instauración de un programa sencillo de intervención dirigido a los pacientes y a sus familiares y la realización de un lipidograma durante las primeras 24 h del ingreso se han mejorado las medidas de prevención secundaria al alta y su mantenimiento a los 6 meses. Se ha constatado una buena aceptación del programa por parte de los pacientes.

Palabras clave: *Infarto de miocardio. Prevención. Fármacos.*

INTRODUCTION

The 4S,[1] CARE,[2] and LIPID[3] studies have shown that lowering cholesterol levels by prescribing statins

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ABBREVIATIONS

CVRF: cardiovascular risk factors.
AMI: acute myocardial infarction.
ACE inhibitors: angiotensin converting enzyme inhibitors.
BMI: body mass index.
LDL: low density lipoprotein.
HDL: high density lipoprotein.

for patients with chronic coronary heart disease reduces rates of all-cause mortality, coronary heart disease mortality and cardiac mortality. Statin therapy also decreases reinfarction rates and the need for heart surgery.

Cardiology Societies believe sufficient evidence exists to prove the relationship between levels of total cholesterol, low density lipoprotein (LDL) cholesterol and cardiovascular risk and recommend maximum doses for medication.[4-6] Beta-blockers,[7-9] angiotensin converting enzyme inhibitors (ACE inhibitors),[10] and antiplatelet drugs[11,12] have also proved beneficial in secondary prevention.

However, a number of patients who should benefit from these findings and recommendations do not actually do so. The PREVESE II study[13] showed that only 29% of patients with myocardial infarction were prescribed statins at discharge, 46% were prescribed ACE inhibitors, and 45% beta-blockers. However, 88% of patients were prescribed antiplatelet drugs, which is a figure much closer to recommendations. The EUROASPIRE II study[14] reported similar patterns in several European countries, as did the US National Registry of Myocardial Infarction[15].

The causes of this appear to be physicians' prescriptions and patients' compliance with treatment. Early prescription would improve the situation. In France, the PREVENIR study[16] showed that 95% of patients prescribed lipid-lowering medication at hospital discharge continued to comply with treatment at 6 months. Statin therapy is the recommended secondary prevention treatment least often prescribed at discharge. This may be due to the spontaneous decrease in cholesterol levels during the acute phase of myocardial infarction and the lack of studies that recommend statins for patients with acute coronary syndrome. However, starting statin therapy in the acute phase of coronary heart disease[18-20] has been demonstrated to have an early beneficial effect on endothelial dysfunction[17] with an almost complete absence of side effects.

Secondary prevention using different, more or less complex interventions can produce significant improvements as recent research has shown.[21-23] The objective of our study was to determine whether heightening the awareness of attending physicians followed by two simple interventions (obtaining lipid levels within 24 hours of admission and providing patients and their families with educational information before discharge) would improve secondary prevention at discharge and at 6-month follow-up.

We also analyzed patient satisfaction with the educational program and recorded adverse cardiovascular events occurring during the 6-month follow-up.

PATIENTS AND METHODS

Almost all hospitals in Spain were invited to participate in this study. Participating hospitals had a cardiology service or section and a coronary or intensive care unit, were able to determine patients' lipid levels on admission, received a minimum weekly average of 5 patients with myocardial infarction and agreed to introduce an intervention program to provide information and health education. Initially, 120 hospitals agreed to participate but 10 were subsequently excluded because data submitted could not be identified or because no follow-up took place. Patient enrolment began in September 1999 in the belief that each center would reach a maximum of 50 consecutive patients within 3 months.

Sample size was calculated according to the percentage of patients who at the time of hospital discharge were able to start statin therapy, bearing in mind the evolution observed in the PREVESE studies,[13] in which the proportion grew from 7% to 30%. In this study, we estimated that statin prescription at discharge might approach 50%. With a sample of 2965 patients this would produce a 95% confidence interval ≥1.8%. We calculated a minimum sample size of 3488 patients on the assumption that prescriptions would continue at 50% for 6 months with new enrolments to compensate for a predicted 15% sample erosion.

For each patient we recorded data of hospital affiliation, cardiovascular risk factors (CVRF) prior to acute myocardial infarction (AMI) including lifestyle variables and work activity, family and personal history of coronary heart disease, results of a simple physical examination (weight, height, blood pressure and heart rate), lipid levels determined within 24 hours and treatment at discharge. We also noted whether or not patients were involved in an intervention program to provide information and health education and the 6-month follow-up visit.

At follow-up, we recorded adverse events and patients underwent physical examination and lipid analysis. Pharmacologic treatment and patient observations on compliance with treatment were recorded as were motives for abandoning medication

and patient evaluation of the intervention program.

The intervention program to provide information and health education was carried out by attending physicians. In individual interviews, patients and family were taught the importance of modifying CVRF, adopting more adequate lifestyle and dietary habits and adhering to prescribed medication regimens. Patients were given printed leaflets containing the same information and small reminder stickers to place strategically around their homes. Patients were informed they would be given 6-month follow-up appointments and that they should undergo lipid analysis. Contact with physicians who would handle the follow-up was limited to the standard practice of each center. This usually consisted of the discharge summary.

Statistical analysis consisted of a descriptive study of baseline data. Categorical variables were expressed as absolute frequencies and percentages and quantitative variables were given as mean and SD. Independent samples were compared using chi-square for proportions and the Student *t*-test for means. The McNemar test was used to compare related sample proportions and the Student *t*-test for repeated measures.

For descriptive purposes, we present the percentages that demonstrate patient satisfaction with the intervention program and the occurrence of cardiovascular events.

Control and statistical analysis of data has been carried out by an independent company (LOGITEST) in collaboration with the study's Scientific Committee which supervised the sequence of patient enrolment in the centers and checked the reliability of the data collected.

RESULTS

A total of 4174 patients discharged from the 110 participating hospitals were enrolled in the study. Distribution of patients by region is shown in Figure 1. We excluded 144 patients who were unidentified or lost to follow-up. The final sample was 4030 patients with an average age of 63.7±11.7 years. Women represented 26.9% of the sample and were significantly older than men (68.2±10.5 vs 62.0±11.7 years). Prevalence of CVRF and differences between men and women appear in Table 1.

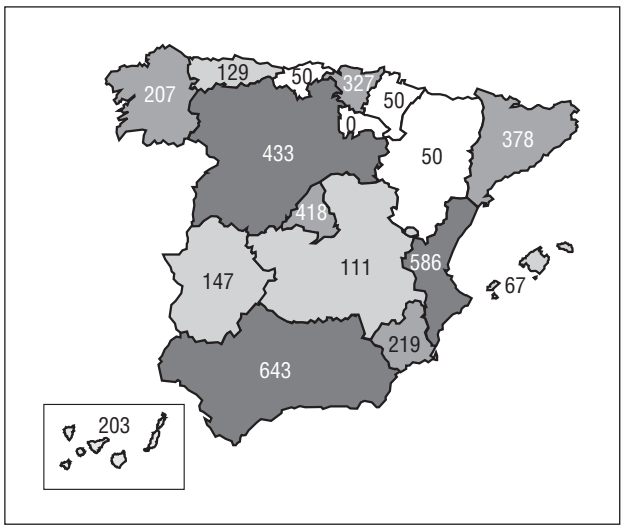

Fig. 1. Distribution of participating patients by region.

Baseline family history data was available for 76% of the sample. We recorded antecedents in the histories of 24.2% of patients. Prior myocardial infarction was recorded for 12.3% of patients, 12.4% had suffered angina of >3 months duration, 3.4% had undergone percutaneous coronary revascularization and 1.6% surgery. A total of 40.3% were in work (44.8% men, 26.9% women).

Average weight of patients was 76.2±11.7 kg (n=3616, 89% of sample), average height was 166.8±7.9 cm (n=3552, 88% of sample) and body mass index (BMI) was 27.4±4.0 (n=3542, 87.8% of sample).

A BMI >25 was defined as overweight and 74.4% of women and 70% of men met this criterion. Obesity (BMI>30) was found in 34.1% of women and 20% of men, with statistically significant differences.

Systolic blood pressure was 133.2±21.4 mm Hg and diastolic blood pressure was 76.9±13.0 mm Hg (n=3891). Heart rate at rest was 72.6±12.4 beats/min. At discharge, 71.1% of patients had controlled blood pressure (≤140-90 mm Hg).

Cholesterol levels were determined within 24 hours for 96% of the sample (n=3896) and fractions were determined for 82% (n=3480): total cholesterol was

TABLE 1. **Cardiovascular Risk Factors by Gender**

	Women	Men	Sample Total	*P*
High blood pressure	694/1008 (68.6%)	1220/2688 (45.4%)	1976/3926 (50.3%)	<.0001
Diabetes mellitus	468/1053 (44.4%)	670/2853 (23.5%)	1170/4020 (29.1%)	<.0001
Hypercholesterolemia	563/1053 (53.5%)	1399/2853 (49.0%)	2016/4020 (50.2%)	.01
Hypertriglyceridemia	186/1053 (17.7%)	367/2853 (12.9%)	578/4020 (14.4%)	.0001
Smokers	133/1027 (13.0%)	1359/2819 (48.2%)	1535/3954 (38.8%)	<.0001

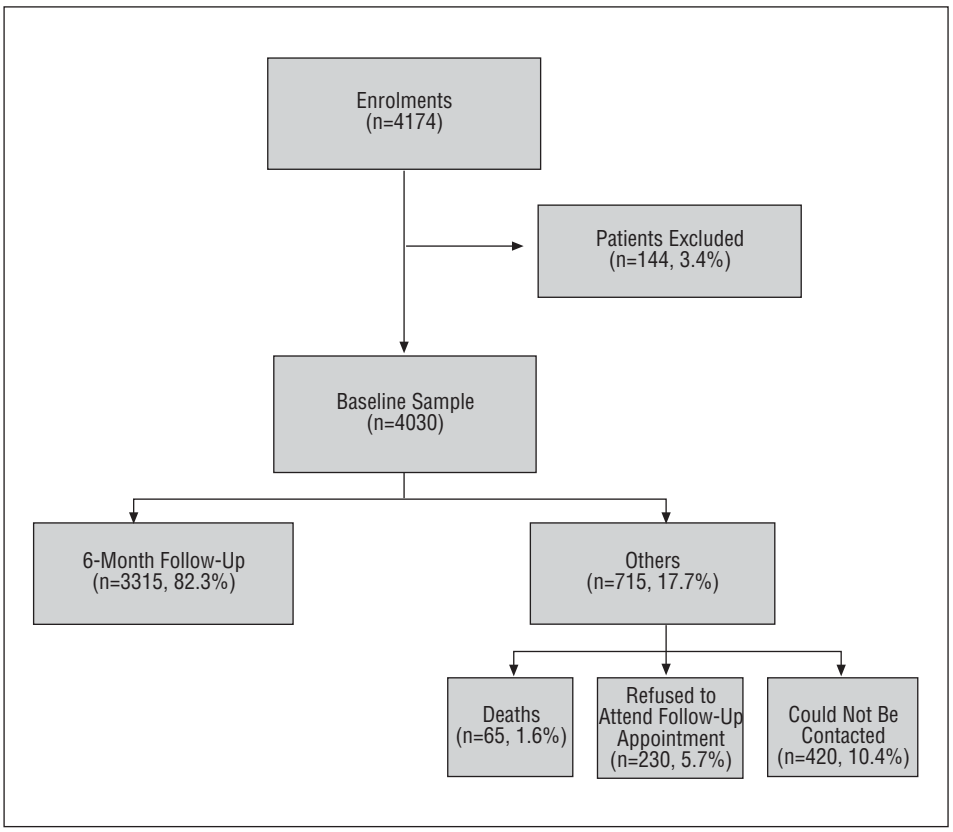

Fig. 2. Flowchart of patients in the study and follow-up

219 (44.9) mg/dL, high density lipoprotein (HDL) cholesterol was 40±11.5 mg/dL, low density lipoprotein (LDL) cholesterol was 154±37.7 mg/dL and triglycerides averaged 156±67.4 mg/dL. Total cholesterol >200 mg/dL was found in 65% of patients and 88% presented low density lipoproteins (LDL) >100 mg/dL. Treatments administered on hospital discharge appear in Table 2. Informative health education interviews were held with 93.2% of patients prior to discharge. These patients also received informative leaflets.

At 6-month follow-up, we received information on 89.9% of the sample. We identified 65 patients who had died (1.6% of those located) and 5.7% refused to attend. We were unable to follow up 420 patients (10.4%) (Figure 2). Table 3 compares baseline data of the 6-month follow-up patients with data of patients lost to follow-up. On average, patients lost to follow-up were significantly older, more of them were women and the percentage of smokers was lower. No significant differences appeared between the groups for patients with diabetes, high blood pressure or average total cholesterol. Patients who died were significantly older and the number of women and patients with diabetes was higher although there were fewer smokers.

In addition to the deaths recorded, we found 2.2% of patients had suffered myocardial infarction, 1.5% had had a heart attack requiring hospitalization, 6.9% had suffered angina requiring hospitalization and 2.9% had undergone revascularization. In all, 11% had required hospitalization.

Table 4 describes significant beneficial changes in a range of parameters in patients attending 6-month follow-up appointments. The survey of lifestyle habits showed that 86.5% of smokers reported they had given up smoking; 71.4% of patients stated they took more exercise than previously; and 77.1% affirmed they had improved their dietary habits.

Table 2 also compares pharmacologic treatment at 6 months with treatment at discharge (n=3193). We found that compliance with prescriptions had been maintained and that levels of prescription were high for statins (88%) and antiplatelet drugs (93.8%). A slight but significant reduction in administration of ACE inhibitors was found but this was balanced by an increase in angiotensin II receptor antagonists and a significant reduction in nitrates, diuretics and anticoagulants. Levels of prescription of beta-blockers were maintained.

Compliance with medication was controlled via patients' statements and non-compliance was defined as not having taken the prescribed dose on one day a week or on 24 days over the 6 months. Non-compliance with medication was reported by 21.1% of patients taking antiplatelet drugs, 21.7% of those

TABLE 2. **Treatments Administered at Hospital Discharge and at 6 Months (n=3193)***

	Discharge		6 Months		*P*
	n	%	n	%	
Resins	13	0.4	15	0.4	NS
Fibrates	43	1.3	35	1.1	NS
Statins	2779	87.0	2809	88.0	.03
ACE inhibitors	1522	47.6	1449	45.3	<.0001
Angiotensin II receptor antagonists	136	4.2	202	6.3	<.0001
Digitalis	89	2.7	90	2.8	NS
Calcium antagonists	574	17.9	651	20.3	<.0001
Beta-blockers	1898	59.4	1884	59.0	NS
Diuretics	440	13.7	403	12.6	.01
Insulin	265	8.3	254	7.9	NS
Oral antidiabetic agents	363	11.3	398	12.4	.005
Anticoagulant agents	195	6.1	137	4.2	<.0001
Nitrates	1341	42.0	1250	39.1	<.0001
Antiplatelet drugs	3007	94.1	2998	93.8	NS
Estrogens	17	1.9	17	1.9	NS
Antiarrhythmic agents	67	2.1	77	2.4	NS

*NS indicates not significant; ACE inhibitors, angiotensin converting enzyme inhibitors.

TABLE 3. **Comparison of Baseline Data of 6-Month Follow-Up Patients With Patients Lost to Follow-Up, and Patients Who Died With 6-Month Follow-Up Patients***

	Follow-Up Patients	Patients Lost to Follow-Up	*P*	Patients Who Died	*P* Versus Follow-Up Patients
Age, years	63.4±11.6	64.5±12.0	.03	72.6±11.7	.0001
Men, %	74.1	69.9	.03	54.7	.0005
Smokers, %	40.1	34.3	.007	19.4	.001
Patients with high blood pressure, %	50.6	47.5	NS	63.1	NS
Patients with diabetes, %	28.5	30.1	NS	49.2	.0003
Total cholesterol, mean	219	218	NS	193	NS

*NS indicates not significant.

taking antihypertensive medication and 28% of patients ta-king lipid-lowering drugs. Patients stated non-compliance was due to side effects (3.8%), forgetfulness (7.6%), thinking the medication was no longer necessary (2.1%) and other causes (2.9%).

The majority of patients (89.2%) believed the intervention program had persuaded them to adopt a healthier lifestyle; 92.3% thought it improved their understanding of the importance of complying with therapy; and 92.8% considered it had helped them follow their medication regimen more assiduously. In addition, 87.7% said the informative leaflet was easily understood and 87.3% considered it had provided useful information about their illness.

DISCUSSION

Our results represent an improvement on the PREVESE II study[13] which did not involve any specific intervention. The most striking improvement has been the increase in the prescription of statins, which has risen from 30% to 88%. The difference in lipid values, which were much higher in this study as they were determined within 24 hours of myocardial infarction, may have influenced this increase.

TABLE 4. **Variation in Parameters of Physical Examination at 6 Months***

Parameter	No.	Baseline	6 Months
Weight, kg	2884	76.3	74.5
BMI	2836	27.3	26.7
SBP, mm Hg	3135	133.3	129.8
DBP, mm Hg	3135	77.2	75.5
Total cholesterol, mg/dL	3126	219.7	192.5
LDL-C, mg/dL	2584	143.9	118.3
HDL-C, mg/dL	2774	40.0	44.0
Triglycerides, mg/dL	2990	155.8	134.0

*BMI indicates body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; LDL-C, low density lipoprotein cholesterol; HDL-C, high density lipoprotein cholesterol.
All differences were statistically significant at *P*<.0001.

However, we cannot confirm this as the cause of increased statin prescription because no control group was included in the study. The increase in prescriptions may be a consequence of heightened awareness on the part of physicians or the evolution of clinical practice. Notwithstanding, these results suggest that interventions as simple as these can improve secondary prevention in selected samples of patients.

In this context, heightening the awareness of participating physicians may have reminded them of the indication criteria of preventative drugs prescribed at discharge. This is borne out by comparing our results with those of non-intervention studies[13] because we also found a 5% increase in prescription of antiplatelet drugs and a 14% increase in beta-blockers.

If we compare prescriptions at discharge with data from the non-intervention IBERICA 1997 study[24] (considered a model in Spain given its high reliability and 4401 patient population representing all cases of AMI in 7 regions) we find higher levels of prescription of antiplatelet drugs (94.1% vs 91.5%), beta-blockers (59.4% vs 44.5%), and ACE inhibitors (47.6% vs 37.6%).

The increase in statin prescriptions at discharge may have been influenced by the determination of lipid levels during the acute phase of infarction, the confirmation that 88% of patients had LDL cholesterol >100 mg/dL, and the steady increase in information about the safety and efficacy of statins in acute coronary syndromes.[17-19] At 6 months, the early use of statins in our study was responsible for significant reductions in average total cholesterol and LDL cholesterol levels, and the values obtained were much closer to those recommended in secondary prevention. However, as we have indicated, the evolution of clinical practice may have played a part in achieving these results. The EUROASPIRE II study,[14] despite its lack of an intervention program, also found a considerable increase in prescriptions by comparison with data from their earlier study.[25]

Significant increases in the use of aspirin (rising from 68% to 92%), beta-blockers (from 12% to 62%), ACE inhibitors (from 6% to 58%), and statins (from 6% to 86%) were achieved by a similar intervention study based on a smaller patient sample.[23] Post-AMI patients were informed about the illness and CVRF control and attending physicians were advised to start preventative treatment prior to discharge.

Other parameters of clinical examination have also been seen to improve significantly (Table 4) with decreased average values for blood pressure, weight and BMI, as well as the favourable modifications in lipid levels mentioned. Some 75% of patients said they took more physical exercise and followed a healthier diet, although 13.5% of smokers had either not given up or had started smoking again.

Adherence to pharmacologic prescriptions in secondary prevention fundamentally depends on recommendations given at discharge, as shown by the PREVENIR study[16] which confirms our data. Differences in the prescription of statin therapy after myocardial infarction between a group of patients who received treatment at discharge and a similar group who did not (88% vs 30%) were made evident in a recent publication[26].

Different intervention programs have improved secondary prevention measures adopted by physicians and patients. In the United Kingdom,[21] a special program of nurse-led clinics in primary care was responsible for substantial improvements in treatment compliance and CVRF control (blood pressure, lipid levels, physical exercise, diet), and only failed in relation to smoking. Similarly, a personalized system of 3 monthly reminders to physicians increased the use of statins from 47% to 85%, reducing LDL cholesterol values to 41%.[22] In our study, we monitored compliance via patient statements and achieved almost 80% success. In addition, some 90% of patients confirmed that the educational program had helped them follow the medication regimen and improve lifestyle habits.

In 15.9% of patients we recorded some form of adverse cardiovascular event during follow-up, with a mortality rate of 1.6%. The Swedish RIKS-HIA registry,[20] including >19 000 patients discharged following AMI, reported a 4% one-year mortality rate among patients who received early statin therapy (29% of the total) by comparison with 9.3% mortality among the rest of the population. Our study did not include a control group of non-intervention patients but the mortality rate does seem similar to that reported for statin therapy patients in the Swedish registry.[20] However, sample erosion in the follow-up (10%) detracts from the value of our data. In contrast, the Spanish PRIAMHO registry[27] of 5242 patients with AMI without any secondary prevention intervention reported 7.6% one-year mortality after discounting patients who died during hospitalization.

A recently published, open, randomized, prospective study[28] of intended treatment shows that patients with coronary heart disease whose LDL cholesterol is held at ≤100 mg/dL for 3 years reduce their all-cause risk of death by 43%, risk of death due to cardiac event by 47% and risk of non-fatal infarction by 59% when compared with a similar population receiving standard attention to cholesterol levels.

These data would suggest that early lipid-lowering treatment in secondary prevention may reduce adverse events, although results of clinical trials have yet to be published.[29,30]

LIMITATIONS OF THE STUDY

A wide range of hospitals from all over Spain participated in this study with no prior sampling or randomization. The high level of participation was intentional as we wanted to demonstrate that an intervention program to provide information and health education could easily be introduced in numerous hospitals.

Data on some of the parameters (level of physical activity, diet, treatment compliance) have been obtained without using quantitative instruments which would have complicated managing the registry. However, patient statements about these parameters were congruent with data on weight loss and reduced BMIs, and reduced lipid values were consistent with the prescription of statins.

A total of 715 patients (17.7%) could not be located or refused to attend follow-up appointments and the majority of them were women or older patients. This loss of patients during the follow-up may be linked to a lower level of compliance. Consequently, our results can only be applied to those patients who followed the advice given in the program.

The absence of a control group of hospitals clearly limits the value of our conclusions. We have described changes as a consequence of our intervention program by comparison with other studies but we recognize that other factors may have been involved. A further study involving a control group of non-intervention hospitals is needed to confirm these results.

CONCLUSIONS

In spite of the limitations mentioned, our results suggest that a simple intervention program centered on a wide-ranging group of selected patients who have survived an AMI and whose lipid levels have been determined within 24 hours can produce an improvement in secondary prevention and maintain favorable results over the first 6 months.

Our simple program was widely accepted by patients, most of whom believed it helped them maintain lifestyle changes and adhere to medication regimens.

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