Randomized Clinical Trial of the Effectiveness of a Home-Based Intervention in Patients With Heart Failure: The IC-DOM Study

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Introduction and objectives. The objective of this study was to determine whether a home-based intervention can reduce mortality and hospital readmissions and improve quality of life in patients with heart failure.

Methods. A randomized clinical trial was carried out between January 2004 and October 2006. In total, 283 patients admitted to hospital with a diagnosis of heart failure were randomly allocated to a home-based intervention (intervention group) or usual care (control group). The primary end-point was the combination of all-cause mortality and hospital readmission for worsening heart failure at 1-year follow-up.

Results. The primary end-point was observed in 41.7% of patients in the intervention group and in 54.3% in the control group. The hazard ratio was 0.70 (95% confidence interval [CI], 0.55-0.99). Taking significant clinical variables into account slightly reduced the hazard ratio to 0.62 (95% CI, 0.50-0.87). At the end of the study, the quality of life of patients in the intervention group was better than in the control group (18.57 vs 31.11; $P<.001$).

Conclusions. A home-based intervention for patients with heart failure reduced the aggregate of mortality and hospital readmissions and improved quality of life.

Key words: *Heart failure. Hospital readmission. Mortality. Quality of life.*

Ensayo clínico aleatorizado para evaluar la efectividad de una intervención domiciliaria en pacientes con insuficiencia cardiaca: estudio IC-DOM

Introducción y objetivos. El objetivo de este estudio es evaluar si una intervención domiciliaria reduce la mortalidad y los reingresos hospitalarios de pacientes con insuficiencia cardiaca y mejora su calidad de vida.

Métodos. Ensayo clínico aleatorizado, realizado desde enero de 2004 a octubre de 2006. Se aleatorizó a 283 pacientes, diagnosticados de insuficiencia cardiaca e ingresados en el hospital, al grupo de atención domiciliaria (grupo intervención) o al grupo de atención habitual (grupo control). La variable principal de resultado se midió al año de seguimiento y fue la combinación de la mortalidad por todas las causas y los reingresos hospitalarios debido al empeoramiento de la insuficiencia cardiaca.

Resultados. La variable principal se observó en el 41,7% de los pacientes del grupo intervención y en el 54,3% del grupo control. La razón de riesgos (HR) fue 0,70 (intervalo de confianza [IC] del 95%, 0,55-0,99). Incluyendo variables clínicas relevantes, la razón de riesgos disminuyó ligeramente (HR = 0,62; IC del 95%, 0,50-0,87). Al final del estudio, los pacientes del grupo intervención tenían una mejor calidad de vida que los pacientes del grupo control (18,57 frente a 31,11; p < 0,001).

Conclusiones. Una intervención basada en la atención domiciliaria en pacientes con insuficiencia cardiaca reduce el conjunto de mortalidad y reingresos hospitalarios y mejora la calidad de vida.

Palabras clave: *Insuficiencia cardiaca. Reingresos hospitalarios. Mortalidad. Calidad de vida.*

INTRODUCTION

Heart failure causes elevated morbidity and mortality and entails considerable public health expenditure.[1,2] Hospital admissions could be averted in this population if patients were better familiarized with their disease and its treatment, and therapy appropriately prescribed.[3]

The aim of home care programs for heart failure patients is to reduce the number of hospitalizations and improve the patients' prognosis and quality of life. To date, the published studies on this subject have used heterogeneous designs (some with very small samples) and shown differing results. Some of these studies have reported that home care interventions can decrease the number of unscheduled readmissions[4,5] for heart failure and reduce mortality.[6,7] Others have additionally shown that these interventions are cost effective.[8] In contrast, some studies found no significant results for preventing readmissions or reducing mortality.[9,10]

A review conducted by the Cochrane Collaboration reported that there is little evidence supporting a relationship between the various interventions carried out (follow-up of patients after hospital discharge, including telephone contact and home visits) and a reduction in hospital admissions for heart failure, although the evidence was more substantial when the analysis was restricted to higher-quality studies (hazard ratio [HR] =0.68; 95% confidence interval [CI], 0.46-0.98; P=.04).[11] One recently published clinical trial has shown that management of moderate to severe heart failure by nursing professionals in hospital units or at the patient's home does not reduce mortality or the number of hospital readmissions when compared to the usual follow-up.[12]

The efficacy of these home interventions should be verified by programs in countries with different health systems, as the scientific evidence regarding their effectiveness remains uncertain. The aim of this study was to evaluate whether a home intervention carried out by nursing professionals reduces mortality and hospital readmissions, and improves the quality of life of patients with heart failure.

METHODS

Design

This is an open, randomized, controlled, clinical trial designed to evaluate the effectiveness of a home intervention. Patients were recruited from January 2004 to September 2005 by well-trained nurses at 2 university hospitals (Internal Medicine Department of Hospital Vall d'Hebron and Cardiology Department of Hospital Clínic) and 2 community hospitals (Internal Medicine Department of Hospital Dos de Mayo and Cardiology Department of Hospital General de Vic). The study was approved by the ethics committee for clinical research of each participating hospital.

The inclusión criteria for this study were as follows: patients with no age limits, of either sex, hospitalized for suspected heart failure based on dyspnea with signs of pulmonary or systemic hypertension, consistent with the Framingham criteria[13] (2 major criteria, or 1 major and 1 minor criterion were required); in addition, the diagnosis at hospital discharge had to show heart failure in the first or second position.

Initially, demonstration of cardiac dysfunction by diagnostic tests such as echocardiography or coronary angiography was also considered as a criterion for inclusion. However, in a previous pilot study it was seen that these tests are not systematically performed in all patients diagnosed with heart failure, and for that reason, they were not included in the criteria for participation.

Patients were excluded if they had concomitant diseases and an expected survival of less than 1 year, a cognitive deficit, a possibility of being outside the geographic area during the following year, or participation in a clinical trial within the previous 3 months.

The study nurses interviewed the patients during their hospital stay and obtained their informed consent for participation before they were discharged to home.

At the end of each interview, the nurse telephoned a central data management site (Fundació Institut Català de Farmacología of Hospital Vall d'Hebron) to request random assignment of patients to 1 of the 2 study groups. Randomization was performed by the WINPEPI[14] program, which uses the pseudorandom number generator described by Wichmann et al,[15] and was stratified for each hospital, assigning patients to the home-based intervention or to the usual follow-up protocol.

A standardized questionnaire was used, which included sociodemographic and clinical data, results of the diagnostic tests, and pharmacological treatment received. Health-related quality of life

was evaluated with the specific quality of life in heart failure questionnaire, Minnesota Living with Heart Failure (MLHF),[16] adapted for use in Spain.

Adherence to pharmacological treatment was determined at the end of the study with the Morisky-Green questionnaire, validated in patients with hypertension[17] and widely used in our setting, which contains 4 questions related to medication use. A patient was considered to have good adherence only if all the questions were correctly answered.

The patients' satisfaction with the health care received was assessed with 2 questions having a closed response and a third question rated on an analog scale (0-10). Patients were queried about their satisfaction with the information received concerning their disease and with the role of the health professionals.

Assuming a 55% incidence of the primary endpoint in the control group and an alpha error of .05, a power of 80% was needed for a sample of 280 patients to detect a 17% reduction in the absolute risk, including a loss of 5%.

Intervention

Following hospitalization, patients randomized to the usual care were referred to their family physician and/or referral cardiologist. A visit was scheduled for 1 year after hospital discharge.

Before they were discharged from hospital, patients assigned to the intervention group received information about their disease and the pharmacological and nonpharmacological treatments prescribed, including a booklet containing information on heart failure for patients, specifically published for this study. Monthly visits to the patients' home were scheduled for the entire year. In addition, nurses contacted patients by telephone every 15 days to evaluate their clinical status. At each home visit, patients received an intensive intervention, including education about their disease and recognition of the warning symptoms, and underwent assessment of their adherence to the medication prescribed and lifestyle habits. In addition, the nurse reviewed the medical history from the time the patient had been discharged from hospital or the time of the last home visit, and checked the patient's functional status and vital signs. Following an established protocol, the nurses contacted the patient's family physician or cardiologist when they deemed it was necessary to start a new treatment or modify the existing one. At each visit, the following were recorded: specific information about hospital readmissions, emergency room visits and outpatient visits, data from the physical examination (New York Heart Association [NYHA] functional class, weight, heart rate, edema), clinical warning signs within the last week, compliance with lifestyle changes, adherence to pharmacological treatment, and any changes in the treatment used.

Endpoints

All patients were followed up until October 31, 2006. The primary endpoint of the study was a combination of all-cause death and hospital readmissions due to worsening of heart failure. Secondary endpoints included cardiovascular death, hospital readmissions due to cardiovascular disease (hospital emergencies were not considered), quality of life, adherence to therapy, and satisfaction. Information was compiled on all hospital admissions (copies of hospital discharges were requested from the records services) for both groups at the end of the study. The endpoints were assessed by a committee of clinical events, blinded to the patient's treatment group.

Statistical Analysis

The baseline data and the results were compared by the χ^2 test for categorical variables, the Student t test for continuous variables that followed a normal distribution, and the Mann-Whitney test for variables with a non-normal distribution. Since it was not possible to define the exact moment of an event in all cases, the Turnbull[18] extension of the Kaplan-Meier procedure was used for interval-censored data to estimate the cumulative probability of experiencing a specific event. This analysis was performed using the routines developed by Fay[19] in the R package.[20] A survival analysis was carried out with the primary endpoint, using a parametric model based on the Weibull distribution. The effect of the covariables in the survival pattern was determined by including them in the Weibull proportional hazards model; the model's goodness-of-fit was assessed according to the residual plots. This parametric approach enabled presentation of the results in terms of the hazard ratio (HR), a convenient measure for the clinical interpretation. The model included the intervention group, prior diagnosis of heart failure, NYHA functional class, diagnosis of chronic obstructive pulmonary disease (COPD), and the visits carried out by the family physician and cardiologist.

The analyses were performed with SAS, version 9.1.3 (SAS Institute Inc., Cary, North Carolina, United States). A P value less than .05 was considered significant. Data were analyzed following the intention-to-treat principle.
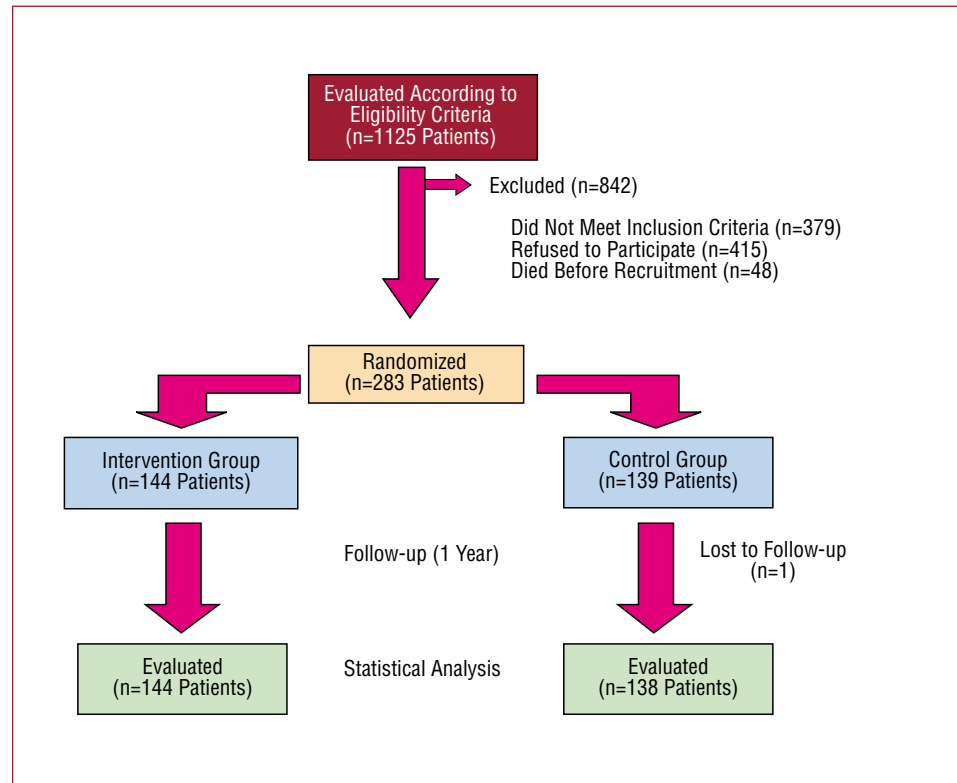
Figure 1. Study flowchart.

RESULTS

The recruitment period lasted approximately 21 months, and 1125 patients were evaluated. Among them, 842 were excluded (74.8%) for various reasons: 45% did not meet the inclusion criteria or had a criterion for exclusion (in 20% the diagnostic criteria for heart failure were not clear, 28% had other concomitant diseases of uncertain 1-year prognosis; 15% had a cognitive deficit or difficulty reading and understanding the information received, 23% were patients from other geographic areas, and 14% had participated in a clinical trial within the last 3 months), 49.3% did not sign the informed consent form, and 5.7% had an end-stage disease or died in the hospital. Ultimately, 283 patients were randomized and 282 (99.6%) reached completion of follow-up at the end of the study (Figure 1).

The characteristics of the randomized patients are shown in Table 1. The 2 groups were similar except for the incidence of COPD. The patients' mean age was 76.3 (8.2) years, and 55.1% were women. The severity of heart failure according to the NYHA classification was class I-II in 25 (8.8%) patients and class III-IV in 253 (89.4%) patients.

In addition to the home visits performed only in the intervention group, patients were seen by primary care physicians, cardiologists outside the hospital, or cardiologists in the hospital outpatient clinics. Among the total, 31.8% of patients in the intervention group and 33.8% in the control group were seen only by family physicians, whereas 4.9% and 5.8%, respectively, were seen only by cardiologists. In addition, 50% of patients in the intervention group and 36% in the control group were visited by both types of specialists during the follow-up period (P=.023). The treatments prescribed at completion of follow-up are shown in Table 2. There were no significant differences between the groups, although there was an overall decrease in angiotensin-converting enzyme inhibitors (ACEI), an increase in angiotensin II receptor antagonists, a considerable increase in spirolactone, and a slight increase in beta-blockers.

Kaplan-Meier survival curves are shown in Figure 2. The primary endpoint events occurred in 60 (41.7%) patients in the intervention group and 75 (54.3%) in the control group (HR=0.70; 95% CI, 0.55-0.99; P=.043). Inclusion of relevant clinical variables, such as a prior diagnosis of heart failure, NYHA functional class, and presence of COPD, resulted in a slight increase in the HR (0.62; 95% CI, 0.50-0.87; P=.0086). Inclusion of the variable visits with the family physician and cardiologist did not change the HR.

A smaller number of total deaths (without statistically significant differences) was observed in the intervention group than in the controls (26

TABLE 1. Comparison of Baseline Data Between Patients in the Intervention Group and the Control Group

Demographic/Clinical Variables	Intervention Group (n=144)	Control Group (n=139))
Women, n (%)	78 (54.2)	78 (56.1)
Age, mean (SDS), y	76.6 (7.5)	76 (8.9)
Living alone, n (%)	30 (20.8)	25 (18)
Heart failure (NYHA class) at the time of hospitalization, n (%)		
I	3 (2.1)	2 (1.4)
II	8 (5.6)	12 (8.6)
III	62 (43.1)	48 (34.5)
IV	68 (47.2)	75 (54)
Unknown	3 (2.1)	2 (1.4)
Heart failure (NYHA class) at hospital discharge, n (%)		
I	61 (42.4)	77 (55.4)
II	75 (52.1)	52 (37.4)
III	7 (4.9)	8 (5.8)
IV	1 (0.7)	2 (1.4)
Ejection fraction, %		
<30%	14	18
30%-39%	24	18
40%-49%	21	21
>50%	40	43
Previous diagnosis of heart failure, n (%)	96 (66.7)	75 (52.1)
Etiological classification of heart failure, n (%)		
Hypertension	92 (63.9)	94 (67.6)
Coronary disease	64 (44.8)	57 (41.3)
Valvular disease	60 (41.7)	62 (44.6)
Others	82 (56.9)	70 (50.4)
Unknown	7 (4.9)	4 (2.9)
Comorbidity, n (%)		
History of myocardial infarction	36 (25)	25 (18)
COPD	49 (34)	28 (20.1)b
Hypertension	112 (77.8)	104 (74.8)
Diabetes	63 (43.8)	57 (41)
Pharmacological treatment at discharge, n (%)		
Angiotensin-converting enzyme inhibitor	80 (55.6)	83 (59.7)
Angiotensin II receptor antagonists	28 (19.4)	25 (18)
Loop diuretics	132 (91.7)	126 (90.6)
Spironolactone	20 (13.9)	17 (12.2)
Beta-blockers	43 (29.9)	44 (31.7)
Oral anticoagulation	68 (47.2)	70 (50.4)
Antiplatelet medication	62 (43.1)	58 (41.7)
Digoxin	49 (34)	48 (34.5))

COPD indicates chronic obstructive pulmonary disease.
[a]In 23% of the intervention group and 25% of the control group, the ejection fraction was not recorded.
[b]$P=.01$.

and 29, respectively), as well as fewer hospital readmissions for heart failure (nonsignificant differences) in the intervention group as compared to the controls (52 and 62, respectively).

Nineteen patients died of a cardiovascular cause in the intervention group and 20 in the control group. The mean number of readmissions due to heart failure in the intervention group was 1.01 and in the control group, 1.3 (nonsignificant differences).

Complete information on quality of life was recorded in 198 (70.2%) patients. The MLHF scores at 1 year decreased in both groups (31 points in the intervention group and 19 in the controls). At completion of the study, patients in the intervention group had a better quality of life than those in the control group (mean total score was 18.57 in the intervention group and 31.11 in the control group; difference of the means, 12.5, 95% CI, 7.10-17.97; $P<.001$) (Table 3).

At the end of the study, 86.1% of patients in the intervention group and 75.5% of those in the control group were adhering to the pharmacological treatment prescribed ($P=.057$).

TABLE 2. Pharmacological Treatment at the End of Follow-up

	Intervention Group (n=118), No. (%)	Control Group (n=109), No. (%)
Angiotensin-converting enzyme inhibitors	42 (39.6)	49 (46.7)
Angiotensin II receptor antagonists	30 (28.3)	23 (21.9)
Loop diuretics	98 (92.5)	92 (87.6)
Spironolactone	25 (23.6)	23 (21.9)
Beta-blockers	32 (30.2)	33 (31.4)
Warfarin	54 (50.9)	52 (49.5)
Antiplatelet medication	42 (39.6)	37 (35.2)
Digoxin	35 (33)	32 (30.5)
Lipid-lowering agents	36 (34)	37 (35.2)

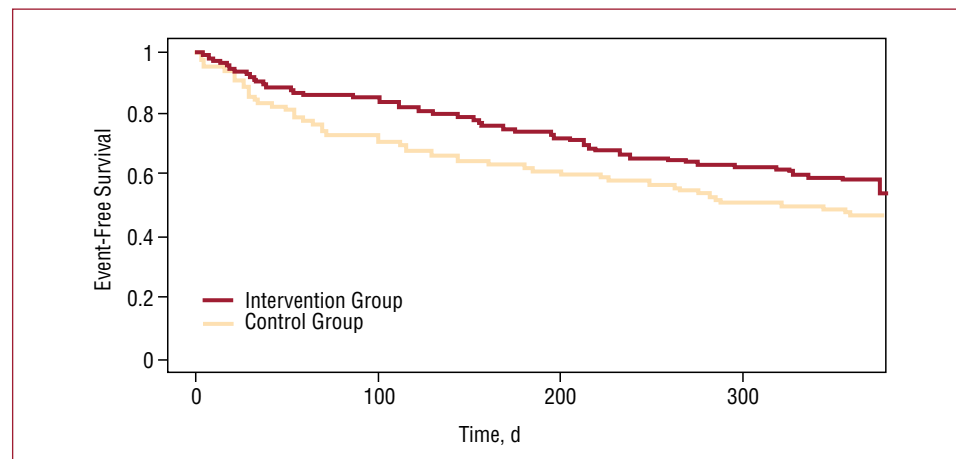Deaths and 1 patient lost to follow-up were excluded from the control group.

Figure 2. Kaplan-Meier Curves showing time to death or hospital readmission in the intervention group and control group.

TABLE 3. Minnesota Living With Heart Failure (MLHF) Scores at Baseline and at 1-Year Follow-up

	Intervention Group		Control Group	
	Score, Mean (SD)	Responders, No.	Score, Mean (SD)	Responders, No.
MLHF				
Baseline	49.05 (12.6)	133	49.91 (14.3)	129
At 1 year	18.57 (13.1)a	101	31.11 (23.9)	97

SD indicates standard deviation.
aStatistically significant differences between the intervention group and the control group: $P<.001$.

Patients in the intervention group were more satisfied with the information they had received about their disease than patients in the control group ($P<.001$) (Figure 3). Patients in the intervention group also had a better perception of the health care providers' concern with their disease than those in the control group ($P<.001$) and showed higher scores in the assessment of the information received about their disease ($P<.001$) (Table 4).

DISCUSSION

The results of this clinical trial indicate that a home intervention carried out by previously trained nursing professionals is effective in reducing overall mortality and hospital readmissions for heart failure, and improves the patient's quality of life, adherence to therapy, and satisfaction with the care received. These results are in keeping with the findings from
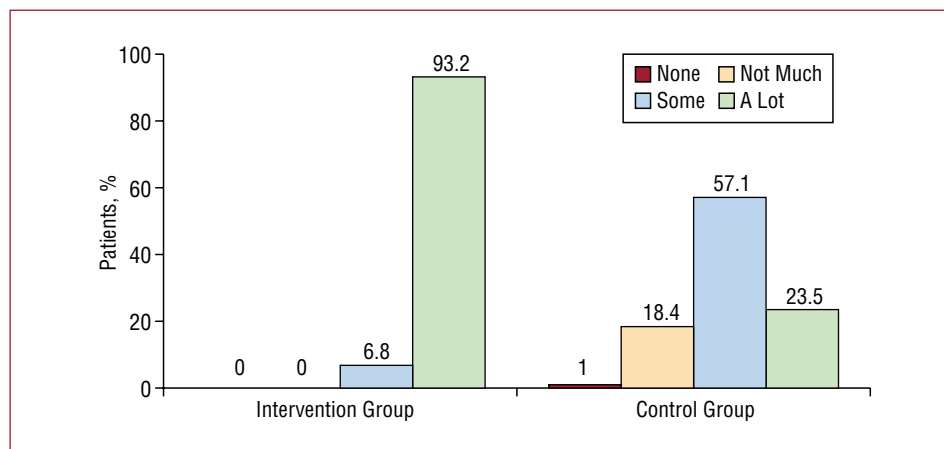
systematic reviews of multidisciplinary programs for the management of heart failure.[21-23]

In the COACH study,[12] no significant differences were observed in morbidity or mortality when a heart failure management program was implemented. In contrast to our study, 50% of the patients were in functional class III-IV at hospital discharge (6%-7% in our study), although at the end of follow-up, a slightly lower rate of events was observed than in our study (overall, 40% vs 46%). This poorer prognosis of our patients can be explained by the higher age of our study population (5 years older on average), and the higher percentage of previous heart failure (60% vs 32%) and comorbid conditions, such as hypertension (75% vs 43%) and diabetes (42% vs 28%). In addition, our population generally received less pharmacological treatment, which could also have had an influence on the prognosis. In our study, the intervention was more intensive (a monthly home visit and telephone contact every 15 days) than that used in the 2 intervention groups in the COACH study, and this might explain why we observed significant differences. Another important variable that could explain the results is the higher percentage of patients who were seen by family physicians and/ or cardiologists in the intervention group than in the controls. Nonetheless, this variable is directly related to the home-based intervention because one of the functions of the nurse was to recommend and facilitate contact with the patient's family physician and cardiologist if, in the nurse's opinion, the patient needed a medical visit. Other heart failure management programs that include telemonitoring systems have recently been shown to improve the clinical results.[24] In addition, an intervention carried out by community pharmacists has demonstrated an increase in adherence to treatment,[25] although another study reported that the effectiveness of this measure in reducing hospital admissions remains uncertain.[26]

TABLE 4. Scores for the Evaluation of Information Received About Heart Failure

Group	Sample, No.	Score, Mean (SD), (Range)
Intervention	103	9.21 (1.08), (6-10)
Control	98	6.25 (1.9), (0-10)
Total	201	7.77 (2.13), (0-10)

SD indicates standard deviation.

The population included in our study had a more severe degree of heart failure at hospital admission according to the NYHA classification than that observed in other studies investigating nurse-led home interventions. Approximately 90% of our patients were classified as NYHA III-IV, compared to 55% of patients in the study by Inglis et al[8] and 49% of patients in the study by deBusk et al.[9] This may be the reason why the number of hospital readmissions for heart failure did not decrease with the intervention. In contrast, in the study by Blue et al,[7] around 80% of patients were classified as NYHA III or IV, and although the sample size was much smaller, the death and hospital readmission rates for heart failure and the HR were similar to those seen in our study. Another study undertaken in Argentina[27] also showed that a simple telephone call by nursing staff to heart failure patients was effective in reducing mortality and hospital readmissions. A Spanish trial with follow-up by telephone contact reported a reduction in hospital readmissions for heart failure at 6 months of follow-up.[28] Another study performed in hospital cardiac units in Spain with a follow-up of 16 months observed a reduction in hospital readmissions and mortality.[29] The same investigators followed up patients for an additional year without offering any specific intervention, and observed that the positive effects on readmissions and mortality disappeared.[30]

The 2 randomized groups in our study were reasonably similar (with the exception of COPD) and the percentage of patients completing follow-up was very high (99.6%). Because of the study design, we were unable to mask the group to which each patient was assigned, and this fact may have introduced some bias in the responses, particularly in those concerning quality of life, adherence, and satisfaction. Nevertheless, an improvement in quality of life was also observed in the control group, which reflects a positive effect of the standard treatment used in these patients. Other studies have also assessed quality of life with the MLHF, although their results do not concur with ours. Investigators using a telephone intervention in the GESICA[27] study reported a less pronounced improvement in quality of life in the intervention group than was found in our study, and a report by Holland et al,[26] which involved a home-based intervention by community pharmacists, surprisingly described a poorer quality of life following the intervention, findings that are difficult to explain. Among the Spanish studies, Falces et al[28] observed no differences in quality of life, whereas Atienza et al[29] did find differences.

We believe that the beneficial effect observed in our study is a direct consequence of the home intervention carried out by specially trained health professionals, although some possible weaknesses should be recognized. One problem with clinical trials is that the endpoint events can be badly classified, and this may have occurred in our study. To avoid this problem, an independent committee was created to blindly evaluate all the events, one by one. When there was a discrepancy, 2 of the study investigators made the final decision. Another possible weakness of the study is related with the intervention itself. Because the intervention consists in a multifactorial approach, we cannot know which of the elements included was more important in reducing mortality and hospital readmissions. Another limitation of the study concerns the generalization of the results. Among a total of 1125 patients initially selected, only 283 (25.2%) were randomized; thus it would be very difficult to extrapolate the study results to the overall population with heart failure. In addition, patients had been admitted to cardiology and internal medicine departments of hospitals having different health care levels and covering different geographical settings. Lastly, in contrast to clinical drug trials, patients in our study were not excluded according to age. Taken together, these characteristics make the patients included on our study more similar to the heart failure patients seen in daily clinical practice than those included in clinical trials.

Despite the limitations described, this study provides new evidence on the benefits of a home-based intervention for reducing morbidity and mortality at 1 year of follow-up in patients with heart failure, performed by nursing professionals who were well trained in the disease under study. It is also interesting to note the improvement in quality of life, adherence to therapy (although a borderline effect with the added limitation that the Morisky-Green questionnaire has been validated in patients with hypertension and not those with heart failure), and satisfaction of the patients, factors that are rarely evaluated in the available published studies.

CONCLUSIONS

An intensive, well-structured, home-based intervention on the part of trained nursing professionals is effective for reducing morbidity and mortality, improving quality of life, and eliciting satisfaction in patients with heart failure.

ACKNOWLEDGMENTS

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