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Home care for heart failure: can caregiver education prevent hospital admissions? A randomized trial in primary care

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Aim **To assess the feasibility and effectiveness of a low-complexity, low-cost model of caregiver education in primary care, targeted to reduce hospitalizations of heart failure patients.**

Methods **A cluster-randomized, controlled, open trial was proposed to general practitioners, who were invited to identify patients with heart failure, exclusively managed at home and continuously attended by a caregiver. Participating general practitioners were then randomized to: usual treatment; caregiver education (educational session for recognizing early symptoms/signs of heart failure, with recording in a diary of a series of patient parameters, including body weight, blood pressure, heart rate). The patients were observed at baseline and during a 12-month follow-up.**

Results **Three hundred and thirteen patients were enrolled (163 in the intervention, 150 in the usual care group), 63% women, mean age 85.3 ± 7.7 years. At the end of the 12-month follow-up, a trend towards a lower incidence of hospitalizations was observed in the intervention group (hazard ratio 0.73; 95% CI 0.53–1.01 $P = 0.061$). Subgroup analysis showed that for patients with persistent/permanent atrial fibrillation, age less than 90 years or Barthel score equal to or greater than 50 a significant lower hospital admission rate occurred in the intervention group (hazard ratio 0.63; 95% CI 0.39–0.99; $P = 0.048$, hazard ratio 0.66; 95% CI 0.45–0.97; $P = 0.036$ and hazard ratio 0.61; 95% CI 0.41–0.89; $P = 0.011$, respectively).**

Conclusion **Caregivers training for early recognition of symptoms/signs of worsening heart failure may be effective in reducing hospitalizations, although the benefit was evident only in specific patient subgroups (with persistent/permanent atrial fibrillation, age <90 years or Barthel score ≥50), with only a positive trend in the whole cohort.**

Trial registration **ClinicalTrials.gov Identifier: NCT03389841.**

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Keywords: atrial fibrillation, caregiver, comorbidity, health education, heart failure, home care

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Introduction

Heart failure is a disease of increasing epidemiological relevance and of high impact on health systems in Western countries, especially for the frail population and the elderly.[1–3] Some patients with heart failure become housebound because of their heart failure, ageing and other comorbidities that cause significant disabilities.

Frequent exacerbations and subsequent hospitalizations contribute to the progression of the disease, worsening the patient's quality of life and increasing costs of healthcare.

It is well known that a significant proportion (up to 50%) of the repeated patient admissions in patients with chronic heart failure are avoidable because they are determined by potentially predictable and preventable precipitating factors.[4] Therefore, careful follow-up and appropriate home patient monitoring by a lay caregiver (spouse, relative, friend or paid helper) may reduce the frequency of patient admissions.

Patients who experience frequent exacerbations are generally at an advanced stage of illness and are assisted at home in a healthcare setting of varying complexity. In Italy, home care can be 'informal', when home visits are only on request or on the initiative of the general practitioner, or 'formal', when home visits are programmed. In the latter case, the assistance can be carried out only by general practitioners (programmed home care), or by the general practitioners and other health professionals (integrated home care).

Many patients with heart failure are looked after by a lay caregiver who could solicit health interventions such as general practitioner or cardiologist home visits, or acute

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hospital admission when there is a significant change or worsening of the patient's condition. The role of the caregiver is, therefore, crucial as they may detect symptoms and signs of imminent exacerbation and can activate the therapeutic measures aimed to prevent the hospitalization.

We planned a research project with the primary objective of assessing whether an educational intervention aimed at increasing the caregiver's skills, combined with the availability of simple and low-cost diagnostic instrumentation, could be able to reduce hospital admissions for any cause in patients with health failure assisted at home. The secondary objective was to verify if this type of intervention is able to reduce hospitalization and mortality for general or cardiovascular causes.

Methods

A cluster-randomized, controlled, open study, approved by the Local Ethic Committee, was carried out. The trial was registered on ClinicalTrials.gov (Identifier: NCT03389841). The General Practitioners of Modena Local Health Authority were invited to participate, provided that they had at least 800 patients and that at the start of the study they had at least one patient with heart failure assisted at home. General practitioners who agreed to participate were randomly assigned to two groups: intervention group, whose patients were assisted in accordance with the procedures established by the project; control group, whose patients continued to be assisted in the usual modality.

Participants were randomly assigned following a simple randomization procedure to one of two treatment groups.

The coordinator of the study (M.S.P.) numbered progressively the general practitioners in enlistment order.

The randomization procedure was carried out by one of the authors (L.A.) who was blinded to the enrolment list. She generated a series of 51 unique random numbers between 1 and 101 by means of an Excel spreadsheet and then assigned them to the intervention group.

All general practitioners produced a list of their patients for whom the diagnosis of heart failure, formulated according to the current diagnostic criteria, was reported in the clinical record with the ICD-9-CM code 428. Among these, patients who met the following criteria were included in the study:

(1) adults of any age and sex in New York Heart Association functional (NYHA) classes II, III, IV, assisted exclusively at home;
(2) willingness and ability to sign a written informed consent;
(3) presence of a person who cared for the patient in a prevalent and regular way;
(4) willingness of the caregiver to attend a training meeting.

Patient enrolment began in August 2013, after the start-up meeting with general practitioners and home visiting doctors, and ended in April 2015.

For all patients, an initial home visit was conducted in which the physician explained the rationale of the study, collected the informed consent and registered the following data:

(1) personal, social, anthropometric and clinical data of the patient;
(2) personal and social data of the caregiver;
(3) level of comorbidity evaluated by the Charlson Comorbidity Index[5];
(4) prognosis evaluated by the 3C-HF score[6];
(5) level of autonomy of the patient through Barthel Index[7];
(6) home care modality (formal or informal).

This initial phase was performed equally in the two groups, and required an average of 60 min for each enrolled patient.

The intervention consisted of an educational session for each caregiver, performed during the first home visit, with the aim of improving their ability to recognize early symptoms and signs of heart failure. These caregivers were given basic but complete information about heart failure, by means of an illustrated brochure, and were provided with a diary for recording essential medical parameters, explaining the importance of recording the body weight of the patient, blood pressure, heart rate, as well as any change in therapy, and giving advice on the appropriate considerations on the need for hospitalizations in case of worsening conditions. The Handbook and the Caregiver record book can be found in the Supplemental web-only Appendix, http://links.lww.com/JCM/A145. Moreover, the educational session included space for questions from the caregiver or the patient. The personal education of caregivers at home allowed customization of the intervention and enlargement of it to problems not strictly related to the management of symptoms of heart failure, when deemed appropriate by the physicians or explicitly requested by the caregiver.

Finally an automatic sphygmomanometer with irregular heartbeat detector (Omron M4) was provided to each intervention group patient and the availability of a weighing scale was verified.

This second phase, performed only in the intervention group, required an average of 30 min.

Each patient was observed for 12 months unless deceased or lost to follow-up.

Twelve months after enrolment, a second visit was performed to collect updated clinical data, information about any hospital admission and, in the intervention

group, the diary provided to the caregiver. This last phase required an average of 30 min for each patient.

All the home visits were made by interns in general medicine suitably trained.

Clinical and laboratory data were obtained by drawing on general practitioners' computerized medical records, clinical documentation available at patients' home during initial and final home visits, and on diaries compiled by caregivers of the intervention group. Data on hospitalizations were confirmed by the Hospital Discharge Forms (more details are available in the on-line documents). The physicians that collected the data at home were not blinded to the treatment allocation. Data analysis was performed by statisticians who were blinded to treatment allocation.

With regard to the specific terms used in the present report, home care is defined in Italy as 'informal', when home visits are performed only on request or on the initiative of the general practitioner, or 'formal' when home visits are programmed. In the latter case, the assistance can be carried out only by general practitioners (programmed home care), or by the general practitioners and other health professionals (integrated home care).

Statistical analysis

Assuming a decrease in the incidence of hospital admissions from 25% in the control group to 15% in the intervention group, setting alpha equal to 5% and a power of 80%, taking into account that about five patients per general practitioner would be enrolled and considering an intra-cluster correlation coefficient equal to 5%, a sample size of 300 patients per arm would be needed.

Numerical variables are expressed as mean and standard deviation, categorical variables as absolute values and percentages. Time to event analysis was used to compare the two interventions with regard to: hospitalization (primary outcome); hospitalization or death (secondary outcome). Patients were included in the study starting from enrolment date until the date in which the first hospital admission occurred. The occurrence of death without hospitalization was considered as related to competing events. For hospitalization or death, patients were included in the analysis starting from enrolment until the date in which the first between hospital admission and death occurred. In both analyses, patients who were event-free after 1 year were considered as censored observations.

Hospitalization was defined as unplanned admission to an inpatient unit or ward in the hospital for at least 24 h. Elective admissions or admission for social reasons were not considered as an event corresponding to hospitalization as an end-point.

Kaplan–Meier curves were used to display the cumulative risks of hospitalization or death, whereas cumulative incidence function curves were reported for risk of hospitalization, considering death as a competing event.

The association between the intervention and the outcomes was estimated by using the hazard ratio. The comparison between groups in terms of hospitalization was performed by using Fine and Gray proportional hazards competing risks regression models,[8] whereas Cox proportional hazards regression models were used for hospitalization or death.

The effect of the intervention was also assessed within subgroups of patients. The subgroups considered were: age (≥ 90 or < 90), sex (men or women), home care model (informal or formal), caregiver characteristic (family member or paid helper), NYHA class (III–IV or II), Barthel score (≥ 50 or < 50), persistent/permanent atrial fibrillation (yes or no).

All models were checked for adherence to the proportional hazard assumption, by means of the analysis of Schoenfeld-type residuals. Hazard ratios and their relative 95% confidence intervals were reported. Results were considered statistically significant if their P values were less than 0.05.

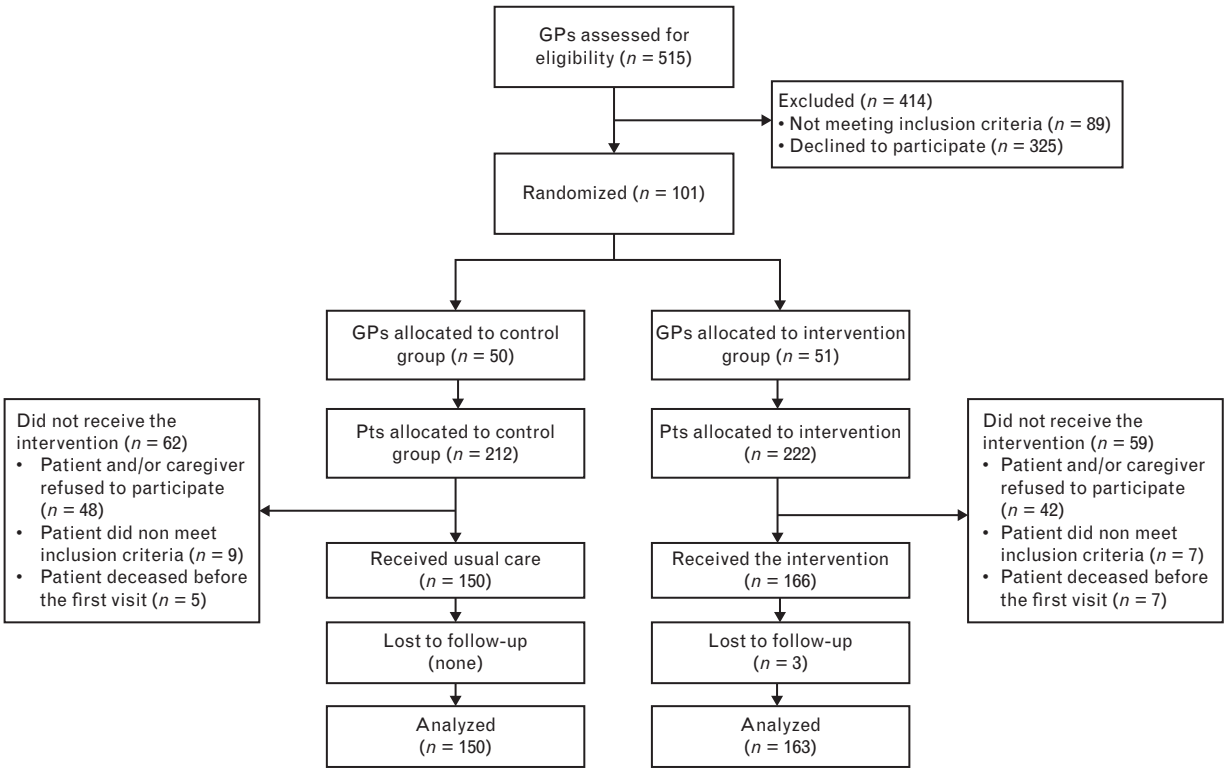
Results

All 515 general practitioners of the Modena Local Health Authority were invited to participate, of whom 89 declared that they did not meet the inclusion criteria and 325 refused to participate (Fig. 1).

One hundred and one general practitioners participated in the study, 50 in the control group, 51 in the intervention group; they reported for the recruitment, respectively, 212 and 222 patients with heart failure assisted at home. One hundred and twenty-one patients were excluded: 62 in the control group, 59 in the intervention group, of which 90 (48 control, 42 intervention) for refusal to participate by the patient himself and/or by the caregiver, 16 (9 control, 7 intervention) for exclusion criteria not reported by the general practitioner, and 12 (5 control and 7 intervention) for death before the first visit. Three patients from the intervention group were lost to follow-up vs. none of the control group.

Overall 313 patients were included: 150 patients in the control group and 163 in the intervention group (Fig. 1). The demographic and clinical characteristics of the patients who refused to participate after allocation were not significantly different from the included patients (data not shown). Table 1 shows the baseline data of the patients enrolled in the two groups. The mean age of control group patients (86.7 ± 5.7 years) was slightly higher than that of the intervention group (84.1 ± 9.0 years), whereas gender distribution was similar. In addition, patients in the control group were more frequently treated with beta-blockers (68.0 vs. 54.0%); considering

Fig. 1



Flow-chart representing the allocation of the patients to the intervention and control groups, respectively.

the key role of this class of drugs in the first-line treatment of heart failure, this difference could be clinically relevant. There were no clinically relevant differences between the two groups concerning the type of assistance, the NYHA class and the prevalence of the main comorbidities.

During the follow-up period, 142 patients had an hospital admission: 66 in the intervention group and 76 in the control group. Overall 86 deaths were observed; 32 of them occurred before the first hospital admission, 18 in the intervention group and 14 in the control group. The number of patients who experienced death or hospital admission was 174; 84 of them were in the intervention group and 90 in the control group.

As shown in Table 2, a trend towards a lower risk of hospital admission in the intervention group was found over time, although it did not reach the significance level (hazard ratio 0.73; 95% CI 0.53–1.01). Similar results were obtained when the occurrence of death or hospitalization was considered (hazard ratio 0.78; 95% CI 0.58–1.05). Cumulative incidence curves for both outcomes are reported in Fig. 2 (panels a and b). The proportional hazards assumption was met by all independent variables in all regression models (data not shown).

In subgroup analysis (Table 3), a lower risk of hospitalization was found in the intervention group as compared with the control in the following subgroups: patients with persistent/permanent atrial fibrillation (hazard ratio 0.63; 95% CI 0.39–0.99); patients with age less than 90 years (hazard ratio 0.66; 95% CI 0.45–0.97); patients with Barthel score equal to or greater than 50 (hazard ratio 0.61; 95% CI 0.41–0.89).

Discussion

Frequent exacerbations and the consequent hospitalizations are the cause of disease progression, worsening quality of life and increasing costs of managing patients with heart failure.[1–3] Optimization of medical therapy is only one of the strategies that can be adopted to reduce the need for patient admission, while the adoption of more or less complex healthcare models based on home management has proven to be at least as effective.[4]

In our work, an individual educational intervention targeted to the family members or the paid helpers and focused on the management of patients with heart failure and, in particular, on the recognition of symptoms and early signs of instability has been evaluated. The study was planned to enrol 600 patients; however, only 313 were objects of the analysis and the smaller-than-

Table 1 Baseline characteristics

	Control group ($N=150$)	Intervention group ($N=163$)	P value
Demographic characteristics of patients			
Age, mean ± SD	86.7 ± 5.7	84.1 ± 9.0	0.002
Female, *N* (%)	93 (62.0)	104 (63.8)	0.831
Caregiver, *N* (%)			
Paid helper	83 (55.3)	73 (44.8)	0.080
Family member	67 (44.7)	90 (55.2)	
Home Care, *N* (%)			
Informal	33 (22.0)	32 (19.6)	0.707
Formal	117 (78.0)	131 (80.4)	
Clinical complexity indicators			
Barthel index, mean ± SD	62.5 ± 32.5	67.4 ± 29.6	0.160
NYHA Classes III and IV, *N* (%)	77 (51.3)	73 (44.8)	0.296
Charlson index, mean±SD	4.7 ± 2.7	4.4 ± 2.3	0.269
Heart failure drugs, *N* (%)			
Beta-Blockers	102 (68.0%)	88 (54.0%)	0.016
ACE inhibitors or ARBs	74 (49.3%)	87 (53.4%)	0.629
MR antagonists	59 (39.3%)	60 (36.8)	0.732
Loop Diuretics	127 (84.7%)	144 (88.3%)	0.431
Other treatments			
Oral anticoagulants	65 (43.3%)	69 (42.3%)	0.948
Cardiovascular comorbidities, *N* (%)			
Hypertension (PA >140/90 mmHg)	59 (39.3%)	75 (46.0%)	0.281
Myocardial infarction	46 (30.7%)	44 (27.0%)	0.554
Persistent/permanent atrial fibrillation	66 (44.0%)	72 (44.2%)	0.999
Peripheral artery disease	47 (31.3%)	49 (30.1%)	0.904
Cerebrovascular disease	59 (39.3%)	55 (33.7%)	0.363
Severe valvular heart disease	25 (16.7%)	26 (16.0%)	0.999
Hemiplegia	10 (6.7%)	12 (7.4%)	0.985
Other comorbidities, *N* (%)			
Depressive disorder	59 (39.3%)	60 (36.8%)	0.732
COPD	28 (18.7%)	38 (23.3%)	0.309
Anemia (Hb <11 g/dl)	44 (29.3)	33 (20.3%)	0.083
Dementia	54 (36.0%)	47 (28.8%)	0.217
Connective tissue disease	15 (10.0%)	18 (11.0%)	0.909
Peptic ulcer disease	9 (6.0%)	8 (4.9%)	0.860
Mild liver disease	10 (6.7%)	9 (5.5%)	0.852
Moderate to severe liver disease	7 (4.7%)	4 (2.5%)	0.450
Moderate to severe CKD	58 (38.7%)	45 (27.6%)	0.051
Diabetes mellitus	52 (34.7%)	54 (33.1%)	0.777
Cancer	25 (16.7%)	27 (16.6%)	0.999
Severe osteoarthritis	40 (26.7%)	38 (23.3%)	0.579
Skin ulcers	21 (14.0%)	12 (7.4%)	0.084
Fecal or urinary incontinence	54 (36.0%)	54 (33.1%)	0.678
Characteristics of general practitioners	($N=50$)	($N=51$)	
Age, mean ± SD	57.0 ± 6.3	57.8 ± 6.5	0.531
Female, *N* (%)	23 (46.0%)	17 (33.3%)	0.272
Group practice, *N* (%)	40 (80.0%)	36 (70.6%)	0.387

ARB, angiotensin receptor blocker; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; MR, mineralocorticoid receptor; NYHA, New York Heart Association functional.

expected sample size has certainly reduced the statistical power of the study. Home care and the activity of general practitioners are settings where the implementation of clinical research with prospective studies and randomized clinical trials is particularly complex, especially for independent nonsponsored research and our study highlights the challenges and the difficulties in performing large-scale trials in this specific 'real world' scenario.[9,10]

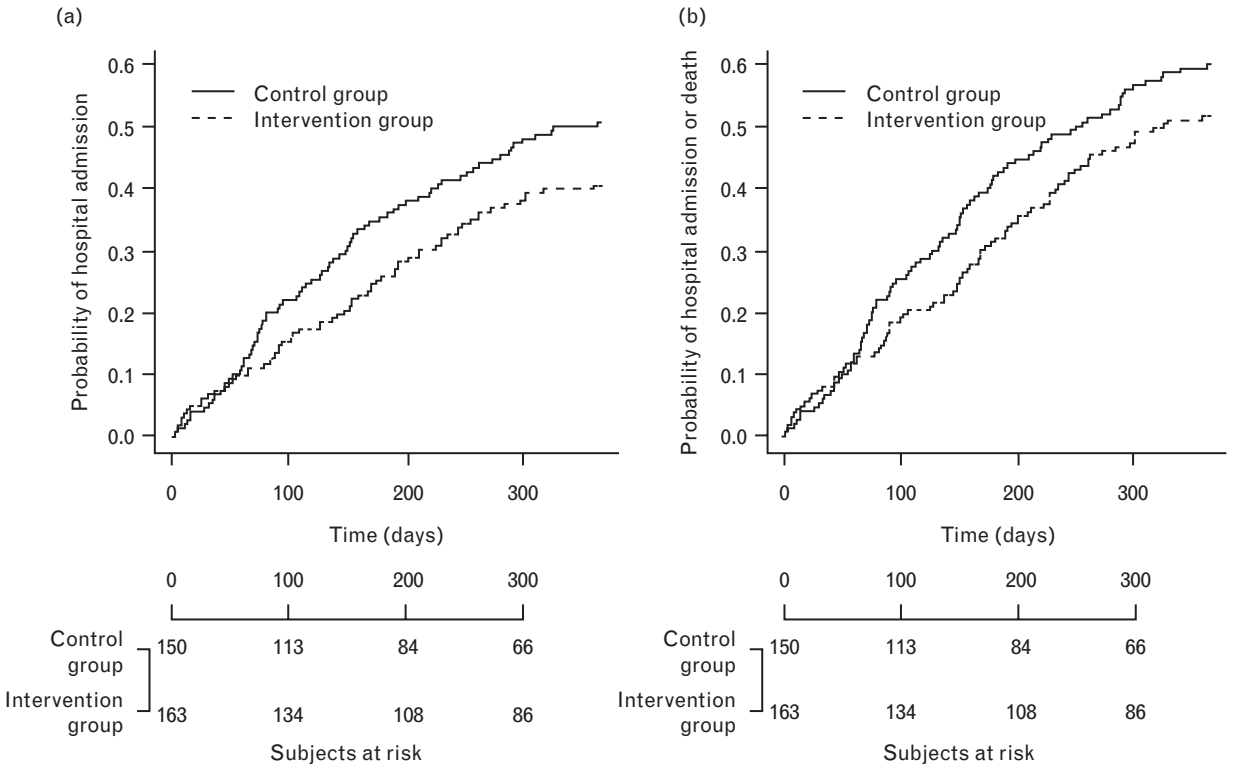
Table 2 Effects of the intervention vs. control on primary and secondary end points

End point	e_I/n_I	e_C/n_C	Hazard ratio	95% CI	P
Hospital admission	66/163	76/150	0.73	0.53–1.01	0.061
Hospital admission or death	84/163	90/150	0.78	0.58–1.05	0.101

e_I, number of events in the intervention group; n_I, number of patients in the intervention group; e_C, number of events in the control group; n_C, number of patients in the control group; 95% CI, 95% confidence interval; P, statistical significance.

In our trial, the educational intervention did not achieve a statistically significant benefit vs. control on hospital admissions or the combined end-point of hospital admissions or death, although a trend towards a benefit appeared over time. The lack of any benefit in the first follow-up period (90–100 days; Fig. 2) combined with the divergence of the curves over time suggests the opportunity for continuing clinical research in this setting, by expanding research to a broader sample of general practitioners, from a regional or national perspective, and with a longer follow-up. It is possible that education of the caregivers requires some time for a full implementation of the care plan and this may explain the lack of any benefit for events occurring in the first follow-up period

Fig. 2



Risk of outcomes: on the left (panel a) hospital admission as first event, on the right (panel b) hospital admission or death.

(presumably related to the most severe patients), but with an emerging incremental effect for events appearing later during follow-up. From this perspective, it is important to consider that education of caregivers was based in our study on two sessions and no formal checks of the level of education actually achieved was planned.

Table 3 Effects of the intervention vs. control on primary and secondary end points, in subgroups of patients

	Hospitalization			Hospitalization or death		
Subgroup	Hazard ratio	95% CI	*P*	Hazard ratio	95% CI	*P*
Sex						
Women	0.69	0.44–1.06	0.090	0.78	0.53–1.15	0.207
Men	0.80	0.49–1.32	0.390	0.79	0.50–1.25	0.315
Caregiver						
Paid helper	0.79	0.49–1.26	0.320	0.90	0.60–1.36	0.630
Family member	0.70	0.44–1.12	0.140	0.71	0.46–1.10	0.125
Home care model						
Informal	0.90	0.48–1.68	0.740	0.97	0.53–1.80	0.935
Formal	0.69	0.47–1.02	0.060	0.74	0.52–1.04	0.080
NYHA class						
II	0.89	0.54–1.46	0.640	0.96	0.61–1.50	0.850
III and IV	0.65	0.42–1.02	0.059	0.68	0.46–1.02	0.061
Persistent/permanent atrial fibrillation						
No	0.84	0.53–1.34	0.460	0.84	0.55–1.28	0.412
Yes	0.63	0.39–0.99	0.048	0.72	0.47–1.10	0.130
Age						
<90 years	0.66	0.45–0.97	0.036	0.78	0.54–1.12	0.179
At least 90 years	0.88	0.47–1.65	0.690	0.84	0.50–1.42	0.517
Barthel score						
<50	1.10	0.59–2.04	0.770	1.05	0.62–1.77	0.858
At least 50	0.61	0.41–0.89	0.011	0.70	0.49–1.01	0.052

95% CI, 95% confidence interval; NYHA, New York Heart Association functional; *P*, statistical significance.

Our explorative subgroup analysis seems to suggest that some patient characteristics (age below 90, and more preserved profile of activities of daily living as expressed by the Barthel index) are associated with a significant benefit of the intervention vs. control. Although we are well aware of the limitations of subgroup analysis, these findings may suggest that the search for the 'ideal responders' to an educational intervention for heart failure targeted to caregivers should consider that the extremely elderly patients and those with more compromised disability in daily living activities can get very limited benefit or no benefit, presumably because in these subgroups of patients, heart failure is only one component of a complex clinical scenario, with multiple comorbidities conditioning a very severe functional impairment and a poor outcome. A more comprehensive and personalized approach targeted not only to heart failure but to a series of chronic diseases and disabilities should be more appropriately considered in these cases.

Atrial fibrillation is strictly linked to heart failure[11–13] and strategies for rate control may lead to heart failure improvement and avoidance of hospitalizations.[14,15] In this perspective, the improved surveillance of the caregiver, with periodic check of heart rate, may explain the

benefit of the tested intervention in the subgroup of patients with persistent/permanent atrial fibrillation, who accounted for 44% of this population, in line with the epidemiological profile of atrial fibrillation.[16]

Comparisons with previous literature

A recent Cochrane review[17] examined 25 articles, including 5942 patients, which tested various models of intensive home care services for patients discharged from the hospital with a diagnosis of heart failure, based on the intervention of dedicated nurses or managed directly by the same hospital that had treated the patient. The multiplicity and variety of the interventions considered and of the comparison models make it impossible to draw unequivocal conclusions. However, the results showed the effectiveness of out-of-hospital management of heart failure, mainly based on telephone follow-up by a care-manager nurse, on the incidence of hospitalizations (−25% at 12 months) and on mortality for all causes (−34% at 12 months). On the other hand, intensive hospital-based interventions do not seem to have the same effectiveness.

In some studies,[18,19] special attention has been paid to the education of the patient and the family, in the context of a more structured care intervention, with interesting results in terms of the reduction of admissions, quality of life and welfare costs.

An observational study carried out in Italy[20] also reported a 6% reduction in hospitalization through a telephone follow-up conducted by a care-manager nurse, although with very variable results among the various participating centres.

Our study is in line with the current perspective supporting the institution of networks for the care of outpatients with heart failure,[21–24] taking into account the complexity of the disease, of comorbidities and patient profiles, as well as the need for appropriate referral to specialized centres for candidacy to effective medical and interventional treatments.[24–31] To our knowledge, no other experiences considered heart failure patients followed exclusively at home, not necessarily with a recent admission, testing the effectiveness of a simple, low-cost care intervention, managed exclusively with the resources of the primary care and with simple technological support, with a specific focus on the caregiver, a key figure of the Italian home care system.

Strengths and limitations

As far as the authors are aware, this is the first randomized controlled clinical trial that has tested the possibility of reducing the repeated hospital admission of patients suffering from heart failure by means of a simple, low-cost, intervention, based on the education of the caregiver, totally managed by primary physicians.

The study, however, also has many limitations. In addition to the small sample size, having randomized the general practitioners and not the individual patients in the two treatment arms may have caused an unbalance of possible confounders. Patients in the control group were slightly older than the treatment group and more frequently treated with beta-blockers. The diagnosis of heart failure was not formulated on the basis of predefined criteria but was derived from the clinical records of the general practitioners. However, in all cases, these diagnoses were shared with a cardiologist and, in any case, they reflect usual clinical practice in a 'real life' context. Another potential limitation may consider that in our study the education of caregivers was based on two sessions and no formal checks of the level of education actually achieved were planned. As a matter of fact, the need for caregiver education needs to be afforded according to available resources, and our approach consisted in fact of a low-cost intervention without any compensation for the participating physicians. An alternative model, not applied in our study, may imply verifications of the level of caregiver education achieved, with additional meetings if needed. This can be the object of future investigations.

With regard to the organizational level, the collection of data and the administration of the educational intervention were carried out by general practitioners in training, and this may represent a simple and cheap model that can be applied in any context where young doctors in training are available, thus combining their involvement in medical care with new forms of care delivery. Anyway, in view of the pragmatic nature of this trial, performed without a specific funding, data collection was maintained simple, without planning a prospective collection of any change in treatment as a consequence of caregiver education or caregiver/physician interaction or physicians' evaluations.

Conclusion

In our experience conducting a spontaneous no-profit randomized home-based heart failure trial involving family members or professional carers was extremely difficult, and a high refusal rate for participation led to an underpowered study. However, although previous studies demonstrated that various models of organized home care, generally managed by a team of hospital nurses, can improve patient care and reduce repeated hospital admission of patients discharged with a diagnosis of heart failure, our study was the first to analyse the possibility of obtaining similar results in patients with heart failure, followed at home, even independently from a recent hospital discharge, by applying an intervention focused on the education of the caregiver and using only the resources of the primary carer.

In our cluster-randomized trial, the educational intervention did not achieve a statistically significant benefit vs. control on hospital admissions or the combined end-point

of hospital admissions or death, although a trend towards a benefit appeared over time, with an emerging incremental effect for events occurring late during follow-up. Moreover, our explorative subgroup analysis seems to suggest that some patient characteristics (age below 90, and more preserved profile of activities of daily living as expressed by the Barthel index, as well as presence of persistent/permanent atrial fibrillation) are associated with a significant benefit of the intervention vs. control. Although we are well aware of the limitations of subgroup analyses, these findings may suggest that the search for the 'ideal responders' to an educational intervention for heart failure targeted to caregivers should consider that the extremely elderly patients and those with more compromised disability in daily living activities can get very limited benefit. Presumably, this is because of the fact that heart failure is only one component of a complex clinical scenario, with multiple comorbidities conditioning a very severe functional impairment and a poor outcome. Further studies with larger cohorts are needed to evaluate the home care of heart failure patients based on the education and involvement of the caregivers, although their management in the complex setting of primary care appears quite challenging.

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Conflicts of interest

The authors did not report any conflicts of interest or financial ties to disclose with regard to the topic of the present study. Giuseppe Boriani reported speaker's fees of small amount from Biotronik, Boehringer Ingelheim, Medtronic and Boston Scientific outside the submitted work.

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