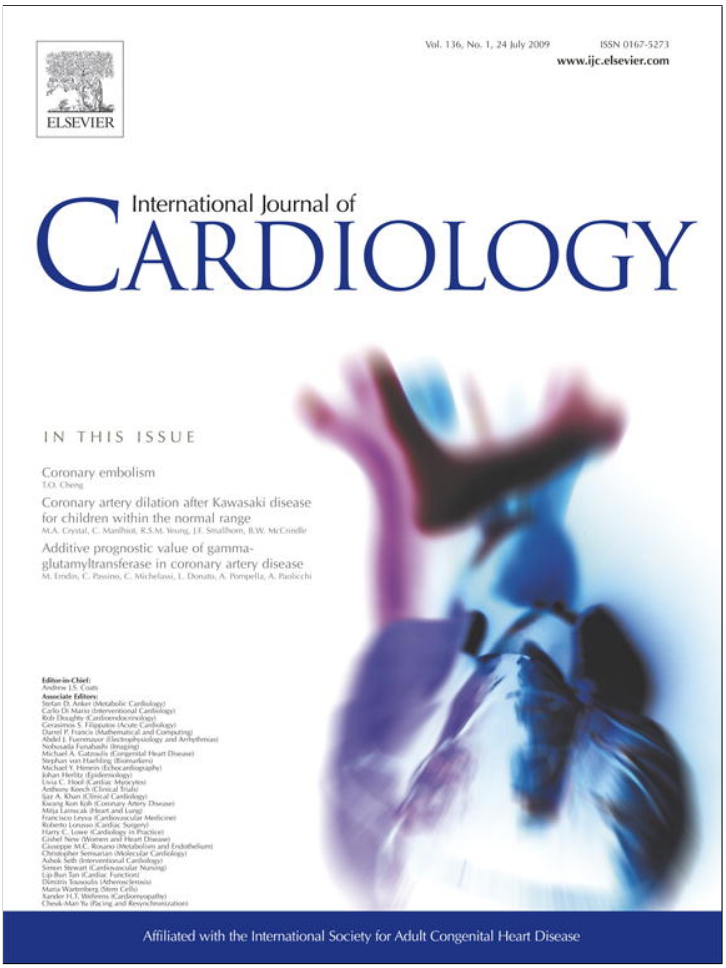

ELSEVIER

International Journal of Cardiology 136 (2009) 56–63

International Journal of Cardiology

www.elsevier.com/locate/ijcard

Morbidity and mortality among heart failure patients in Galicia, N.W. Spain: the GALICAP study

Fernando Otero-Raviña [a], Lilian Grigorian-Shamagian [b], Luis Fransi-Galiana [c], Carlos Názara-Otero [d], José M[a] Fernández-Villaverde [e], Alberto del Álamo-Alonso [f], Enrique Nieto-Pol [g], Miguel de Santiago-Boullón [h], Isidro López-Rodríguez [i], José M[a] Cardona-Vidal [j], Alfonso Varela-Román [b], José R. González-Juanatey [b,*] for the GALICAP Study researchers

[a] *Sección de Coordinación Asistencial, SERGAS, Santiago de Compostela, Spain*
[b] *Servicio de Cardiología, Hospital Clínico, Santiago de Compostela, Spain*
[c] *CS Rúa Cuba, Vigo, Spain*
[d] *CS Casa do Mar, Marín, Spain*
[e] *CS Ribeira, Spain*
[f] *CS Novoa Santos, Ourense, Spain*
[g] *CS Concepción Arenal, Santiago de Compostela, Spain*
[h] *CS Narón, Spain*
[i] *CS Begonte, Spain*
[j] *CS Ventorrillo, A Coruña, Spain*

Received 1 July 2007; received in revised form 30 September 2007; accepted 23 April 2008
Available online 9 July 2008

Abstract

Objective: Characterization of current morbidity and mortality among heart failure (HF) outpatients in Galicia (N.W. Spain), together with their main determinants.
Design: Prospective multicentre study involving 149 primary care physicians.
Setting: Primary care physicians selected randomly from among all (1959) primary care physicians in Galicia.
Patients: Clinical and epidemiological information for 1195 outpatients with HF were collected in 2006, with a mean follow-up of 6.5±1.5 months.
Main outcome measures: Survival rates were calculated by Cox's proportional hazard model.
Results: Mean patient age was 76 years, 48% were male, 82% had a history of arterial hypertension, and 32% ischaemic cardiopathy. Echocardiography had been performed in 67%, showing preserved systolic function in 61%. Ninety-two (8%) died during follow-up [74 (80%) of them from cardiac causes], and 313 (29%) were re-admitted to hospital [230 (73%) of them for cardiac reasons]. Multivariate analysis identified the following independent predictors of cardiovascular death and/or readmission: ischaemic cardiopathy [hazard ratio (HR) 1.76, 95% confidence interval (CI) 1.29–4.40], stroke (HR 1.79, CI 1.18–2.73), oedema (HR 1.49, CI 1.10–2.03), anaemia (HR 1.66, CI 1.21–2.27), deteriorated systolic function (HR 1.62, CI 1.19–2.20), and previous cardiovascular admissions (HR 2.33, CI 1.67–3.24). Residence in the Barbanza district was identified as an independent predictor of survival free from cardiovascular admission (HR 0.56, CI 0.37–0.86).

Abbreviations: ACEI, angiotensin-converting enzyme inhibitor; ARA, angiotensin II receptor antagonist; CI, confidence interval; HF, heart failure; HR, hazard ratio; HT, hypertension; LVEF, left ventricular ejection fraction.

* Corresponding author. Servicio de Cardiología, Hospital Clínico Universitario, Travesía Choupana s/n, 15703 Santiago de Compostela, Spain. Tel.: +34 981950757; fax: +34 981950757.
E-mail address: jose.ramon.gonzalez.juanatey@sergas.es (J.R. González-Juanatey).

doi:10.1016/j.ijcard.2008.04.025

Conclusion: Morbidity and mortality are currently high among Galician HF patients, and their best single predictor is previous hospitalization for cardiovascular reasons.

Keywords: Heart failure; Primary care; Prognosis

1. Introduction

The cardiovascular disease that in recent years has increased most in incidence and prevalence is heart failure (HF) [1,2]. The associated significant increase in health expenditure is directly correlated with repeated admissions to hospital [3–5]. Programmes that coordinate different levels of medical and nursing care in response to this challenge have been able to prolong survival and improve quality of life while significantly reducing the number of re-admissions to hospital [6–9].

In spite of the advances in prevention and treatment that have been made over the past 25 years, the death rate from HF is high. Recent clinical trials recording annual death rates lower than 10% [10–12] do not reflect the situation of HF patients in general, among whom the death rates observed are usually higher than 20% and can approach 50% in the first year of follow-up [13–15]. This discrepancy is largely attributable to differences such as the greater age and greater prevalence of comorbidity among non-trial patients, and the closer surveillance and better treatment of trial patients.

The GALICAP study was designed to determine the characteristics and short-term prognosis of HF patients in Galicia (N.W. Spain) who have been admitted to hospital with a diagnosis of HF and have subsequently been attended by primary care physicians as well as specialists. It is the first such study to have been carried out in Spain, and we believe that it provides a more realistic picture of HF in our region – and possibly in all Spain – than previous studies: since practically all HF patients here undergo periodic check-ups in primary care centres, the GALICAP sample is representative of the entire HF population and avoids the sampling bias of earlier studies. It is our hope that GALICAP will thus provide a basis for the design of more efficient preventive and therapeutic strategies, in which close coordination of primary and specialist care will no doubt play a fundamental role.

The characteristics of the GALICAP sample upon admission to the study have been published elsewhere [16]. HF outpatients in Galicia are typically of advanced age (mean 76 years), rather more than half are women (52%), 82% have a history of arterial hypertension (HT), 61% [of those examined by echocardiography] have preserved systolic function [left ventricular ejection fraction (LVEF) > 50%], and there is a high prevalence of diabetes and associated pathologies such as atrial fibrillation, kidney failure and anaemia. Here we report morbidity and mortality in the GALICAP sample over an average 6 months' follow-up, together with their main determinants.

2. Patients and methods

2.1. Study protocol

The research team included 149 primary care physicians distributed among eight geographical areas of Galicia in proportion to their populations. Subject to informed consent, they were to record data for their consecutive patients who following admission to hospital at some time for at least 24 h had been discharged with a diagnosis of HF made by a specialist (cardiologist and/or internist). The total number of patients included in the sample was 1195, an average of 8 per physician (interquartile range 6–10). At six-month follow-up, 26 patients (2%) had been lost from the study. The quality of the data was corroborated by internal audit.

2.2. Variables

The data recorded included demographic, anthropometric, clinical and analytical variables; the results of any additional diagnostic tests (echocardiography, coronariography); data on admissions to hospital during the year prior to inclusion in the study; and data generated at inclusion (the results of physical examination, electrocardiography and biochemical tests, and the treatment prescribed). Patients were classified as hypertensive if a diagnosis of HT figured in their medical record, and hypertensives were deemed to have controlled HT if their blood pressure was below 130/80 mm Hg at inclusion [17]. Any echocardiographic and coronariographic data collected were the latest such to have been entered in the patient's medical record.

HF was classified as of ischaemic origin if the patient's record featured a diagnosis of ischaemic cardiopathy; as due to valve disease if associated with at least moderate prior valve dysfunction in the absence of ischaemic cardiopathy; as of hypertensive origin in hypertensive patients with no signs of any other significant cardiopathy; and as idiopathic dilated cardiomyopathy if systolic function was depressed (LVEF < 50%) [18] in the absence of any other cardiopathy.

Readmission to hospital during the six-month follow-up period was deemed to indicate morbidity. An average 6 months after a patient's inclusion in the study, morbidity and post-inclusion survival time were recorded together with the causes of morbidity or death when relevant.

2.3. Statistical analysis

Qualitative variables are presented as absolute numbers and percentages, and quantitative variables as means ± standard deviations. The statistical significance of associations between qualitative variables was estimated using Pearson chi-squared tests, and that of differences between group means using Student's *t* test for independent samples.

Kaplan–Meier survival curves for survival free from re-hospitalization for cardiovascular reasons were constructed for relevant subgroups and were compared using log rank tests. Factors influencing the risk of death and/or readmission to hospital for cardiovascular reasons were identified in the first instance by univariate analyses. Independent predictors of survival free from cardiovascular readmission were identified by Cox proportional hazards regression analysis, and are reported together with the corresponding hazard ratio (HR) and its 95% confidence interval (CI); the variables included in the model were age, sex, educational level, traditional risk factors (HT, diabetes, dyslipaemia, smoking, alcoholism), associated pathologies (ischaemic cardiopathy, atrial fibrillation, syncope, valve disease, pacemaker use, stroke, peripheral arteriopathy, abdominal aneurysm, chronic obstructive pulmonary disease), obesity, New York Heart Association (NYHA) functional class, oedema, anaemia, kidney failure, left ventricular hypertrophy, systolic function (LVEF > or <50%), treatment [diuretics, angiotensin-converting enzyme inhibitors (ACEI), angiotensin II receptor antagonists (ARA), beta-blockers, aldosterone antagonists, calcium antagonists, anti-coagulants, anti-aggregants, digitalis], admission to hospital for cardiovascular reasons in the year prior to inclusion in the study, and geographical area.

All statistical analyses were performed using SPSS for Windows version 14.0. The criterion for statistical significance was a probability of type I error less than 0.05.

3. Results

3.1. Characteristics of the sample

The characteristics of the GALICAP sample upon admission to the study have been published elsewhere [16]. Table 1 summarizes the characteristics of the 1195 patients included in the study. Some 17% of these patients had received a diagnosis of HF in the year prior to their inclusion in the study, and 46% more than 3 years before inclusion. Only 122 patients (10%) were affected by none of the risk factors listed in Table 1.

3.2. Mortality and morbidity

Patients included in the study were followed up for 6.5 ±1.5 months (median 6.3 months). In this time, the total death rate was 7.9%, 80% of these deaths being of cardiovascular origin, and almost 30% of patients were at some time re-admitted to hospital. Table 2 lists more specific data on mortality and morbidity from various causes in the whole sample and among patients who had or had not been admitted to hospital for cardiovascular reasons in the year before the study; there were significant differences between these two groups as regards both all-cause mortality and morbidity. Table 3 lists death and cardiovascular hospitalization rates among subgroups defined on the basis of sex, age and other variables considered in this study; both outcomes exhibited significant association with anaemia and oedema, but neither was significantly influenced by treatment.

The actuarial six-month survival rate was 93.5%, and the probability of survival free from cardiovascular hospitalization 91.5%. The probability of survival free from cardiovascular hospitalization was significantly lower for patients who had been hospitalized for cardiovascular reasons in the preceding year than for those who had not (Fig. 1).

For the combined outcome "death or cardiovascular hospitalization", univariate analyses showed statistically significant relationships with age (HR 1.02, CI 1.01–1.03), HT (HR 1.46, CI 1.04–2.05), ischaemic cardiopathy (HR 1.67, CI 1.31–2.12), atrial fibrillation (HR 1.32, CI 1.04–1.68), kidney failure (HR 1.42, CI 1.04–1.94), anaemia (HR 1.79, CI 1.39–2.30), oedema (HR 1.88, CI 1.48–2.40), NYHA functional class III or IV (HR 1.58, CI 1.24–2.02), coronariography (HR 1.40, CI 1.06–1.84), depressed systolic function (HR 1.42, CI 1.06–1.90), cardiovascular hospitalization in the previous year (HR 2.38, CI 1.86–3.05), and residence in the Barbanza district (HR 0.50, CI 0.35–0.71).

Multivariate analysis with all the univariate analysis variables included in the analysis identified ischaemic cardiopathy, stroke, oedemas, anaemia, depressed systolic function and cardiovascular hospitalization in the previous year as independent predictors of death and/or cardiovascular hospitalization, and residence in the Barbanza district as a predictor of survival free from cardiovascular hospitalization (Table 4). Treatment with beta-blockers was a predictor of survival free from cardiovascular hospitalization among patients aged <70 years.

4. Discussion

Over a six-month follow-up period, the GALICAP study found the overall death rate among Galician outpatients with HF to be 7.9%, 80% of these deaths being of cardiovascular origin. Cardiovascular causes involving de-stabilization of HF were also largely responsible for 30% of patients being re-admitted to hospital during this period. Cardiovascular hospitalization during the previous year, ischaemic cardiopathy, anaemia and clinical signs of severe HF were independent predictors of mortality and/or cardiovascular hospitalization during follow-up. The only drug class emerging as an independent predictor of survival free from cardiovascular hospitalization was beta-blockers, and then only for patients younger than 70 years. As far as we know, GALICAP has been the first Spanish study in which

Table 1
Anthropometric, clinical and treatment characteristics, cardiovascular risk factors, antecedents and associated pathologies in the patients included in GALICAP study sample.

Patients included	1195 (100%)
Sex (F)	623 (52.1)
Age (years)	76±10
Weight (kg)	74.6±14.0
Height (cm)	160.3±9.2
Abdominal girth (cm)	97.6±14.2
BMI	
$\bar{x}$ ±SD (kg/m^2)	29.0±5.0
<20	18 (1.5)
20–25	214 (17.9)
25–30	522 (43.7)
>30	441 (36.9)
Systolic BP (mm Hg)	131±18
Diastolic BP (mm Hg)	76±11
Lower-limb oedema	423 (35.4)
Anaemia	290 (24.3)
NYHA functional class	
I	221 (18.5)
II	574 (48.0)
III	343 (28.7)
IV	57 (4.8)
Aetiology ischaemic	376 (31.5)
Hypertensive	428 (35.8)
Valve disease	293 (24.5)
IDC	18 (1.5)
Other	80 (6.7)
Treatment	
Diuretics	983 (82.3)
Calcium anta gonists	219 (18.3)
ACEIs	574 (48.0)
ARAs	348 (29.1)
Beta-blockers	320 (26.8)
Alpha-blockers	55 (4.6)
Spironolactone	196 (16.4)
Digitalis	449 (37.6)
Nitrates	296 (24.8)
Anticoagulants	548 (45.9)
Aspirin	380 (31.8)
Other anti-aggregants	111 (9.3)
Anti-arrhythmics	94 (7.9)
Statins	519 (43.4)
NSAIDs	49 (4.1)
ARA and/or ACEI	887 (74.2)
ARA and/or ACEI+BB	231 (19.3)
ARA and/or ACEI+BB+Spiro	44 (3.7)
Cardiovascular risk factors	
Arterial hypertension	981 (82.1)
HT with controlled BP	419 (42.7)
Dyslipaemia	557 (46.6)
Diabetes mellitus	370 (31.0)
Smoking	137 (11.5)
Alcoholism	79 (6.6)
Associated pathologies	
Ischaemic cardiopathy	380 (31.8)
Myocardial infarct	217 (18.2)
Revascularization	84 (7.0)
Atrial fibrillation	583 (48.8)
Valve disease	422 (35.3)
Syncope	97 (8.1)
Pacemaker installed	102 (8.5)
Abdominal aneurysm	12 (1.0)
Associated pathologies	
Stroke	131 (11.0)
Peripheral vasculopathy	131 (11.0)
Kidney failure [a]	161 (13.5)
Kidney failure [b]	750 (62.8)
COPD	332 (27.8)
Hospitalization in the previous year	
Total	675 (56.5)
For cardiovascular reasons	537 (44.9)
For HF	379 (31.7)

F, female; BMI, body mass index; $\bar{x}$, mean; SD, standard deviation; BP, arterial blood pressure; NYHA, New York Heart Association; IDC, idiopathic dilated cardiomyopathy; ACEI, angiotensin-converting enzyme inhibitor; ARA, angiotensin II receptor antagonist; NSAID, non-steroid anti-inflammatory drug; BB, beta-blocker; Spiro, spironolactone; HT, hypertension; COPD: chronic obstructive pulmonary disease; HF, heart failure.
[a] Kidney failure as recorded in medical records.
[b] Kidney failure was here taken to be indicated by a glomerular filtration rate lower than 60 ml/min, as calculated using the Cockcroft–Gault formula.

mortality and re-hospitalization in the whole outpatient HF population have been quantified for each major cause with a view to the evaluation of cause-specific cardiovascular risk.

Overall mortality in this study, 7.9% in 6 months, was greater than in recent clinical trials, a finding that was expected for the reasons discussed in the Introduction [10–12]. It was also greater than in the BADAPIC Register of HF patients managed in HF-specific hospital clinics [19], no doubt in part because the mean age of the BADAPIC patients was only 66 years and in part because a greater proportion of BADAPIC patients were treated with drugs of proven benefit for survival. However, the GALICAP death rate is considerably less than that observed in EuroHeart Failure Survey I [20] (13.5% in 12 weeks), and other population studies have even reported annual death rates greater than 30% [15,21].

Few community studies report cause of death for HF patients. In this study 80% of deaths were due to cardiovascular causes, and we observed no significant difference between the number due to refractory HF (30%) and the number of sudden deaths (25%). This latter finding contrasts with the predominance of sudden death in the CHARM [22] and EPHESSUS [23] trials; the discrepancy may be due to the CHARM and EPHESSUS samples having had a greater prevalence of ischaemic cardiopathy than the GALICAP sample, and being composed of patients whose condition was generally more stable.

Another noteworthy feature of the GALICAP data is the high proportion of deaths due to stroke, 12%. This is probably attributable largely to the high prevalence of HT and the advanced age of the sample.

Nearly 30% of our patients required re-hospitalization at some time during the six-month study, and about two-thirds of these re-admissions were for cardiovascular reasons, most of them HF-related. Previous studies of the hospitalization of

Table 2
Gross death and re-hospitalization rates in the whole sample and in subgroups that had (PCVH) and had not (No PCVH) been hospitalized for cardiovascular reasons in the year prior to inclusion in the study.

	Whole sample 1169 (100%)	PCVH 641 (54.8%)	No PCVH 528 (45.2%)	*p*
Gross mortality	92 (7.9)	68 (10.6)	24 (4.5)	<0.001
By cause of death				
Non-cardiovascular	18 (19.6)	16 (23.5)	2 (8.3)	
Cardiovascular	74 (80.4)	52 (76.5)	22 (91.7)	ns
RHF	28 (30.4)	21 (30.9)	7 (29.2)	
SD	23 (25.0)	18 (26.5)	5 (20.8)	
MI	9 (9.8)	5 (7.4)	4 (16.7)	
Stroke	11 (12.0)	5 (7.4)	6 (25.0)	
Others	3 (3.3)	3 (4.4)	0 (0.0)	
Hospitalization	343 (29.3)	239 (37.1)	105 (19.9)	<0.001
Cardiovascular cause	230 (19.7)	163 (25.4)	67 (12.7)	<0.001
Death and/or hospitalization	374 (32.0)	262 (40.9)	112 (21.2)	<0.001
Death and/or cardiovascular hospitalization	275 (23.5)	198 (30.9)	77 (14.6)	<0.001

RHF, refractory heart failure; SD, sudden death; MI, myocardial infarct; ns, not statistically significant.

HF outpatients have reported similar findings [11]. These results highlight the unstable clinical situation of community HF patients, and points to a need for HF care systems that coordinate the actions of the various levels of health care. Where such systems have been implemented they have proved to prolong survival and markedly reduce the number of re-admissions to hospital [3–5], an effect that combines a significant gain in quality of life for the patient with a significant reduction in the main HF-related health cost.

The main causes of HF decompensation are noncompliance with the therapeutic regimen, and retention of sodium and water. In the CHARM study, the death and cardiovascular hospitalization rates among patients taking at least 80% of the prescribed dosage were relatively low regardless of whether they took candesartan or placebo, probably in part because compliance with the drug regimen is highly associated with compliance with other therapeutic measures, both pharmacological and non-pharmacological [24].

Identification of the determinants of the prognosis of a disorder is a first step towards the rational design of strategies for increasing survival and reducing the risk of complications. Depending on the population studied, the prognosis of HF has been reported to be influenced by a wide variety of demographic, clinical, biochemical or therapeutic factors. In the GALICAP study, the best predictor of the combined outcome of death and/or hospitalization within 6 months was hospitalization for cardiovascular reasons in the previous 12 months. Other factors associated with this combined outcome in univariate analyses were age, HT, ischaemic cardiopathy, atrial fibrillation, kidney failure, anaemia, clinical signs of severe HF (oedema and NYHA classes III and IV), and depressed systolic function. Residence in the Barbanza district was associated with longer survival free from hospitalization for cardiovascular reasons. The factors identified by the multivariate analysis as independent determinants of prognosis were hospitalization for cardiovascular reasons in the previous 12 months, ischaemic cardiopathy, anaemia, oedema, depressed systolic function, and residence in the Barbanza district. The influence of residence in the Barbanza district may hopefully be attributed to the fact that the primary care physicians of this district had taken a refresher course in cardiovascular medicine with special emphasis on the management of HF patients, which probably caused a better adherence to the

Table 3
Gross death and re-hospitalization rates in subgroups defined by diverse variables.

	Death rate		Cardiovascular hospitalization rate	
	%	*p*	%	*p*
Sex (M/F)	8.1/7.9	ns	20.8/18.8	ns
Age (<70/≥70 years)	2.0/9.5	<0.001	16.0/20.7	ns
HT (yes/no)	8.5/5.2	ns	20.7/15.6	ns
Diabetes (yes/no)	7.0/8.3	ns	22.2/18.5	ns
Dyslipaemia (yes/no)	7.2/8.4	ns	20.6/18.9	ns
Smoking (yes/no)	6.0/8.1	ns	22.4/19.3	ns
Alcoholism (yes/no)	3.7/8.2	ns	24.7/19.3	ns
Ischaemic cardiopathy (yes/no)	9.7/7.1	ns	28.4/15.9	<0.001
Atrial fibrillation (yes/no)	8.9/6.9	ns	21.9/17.6	ns
Syncope (yes/no)	8.7/7.8	ns	26.1/19.1	ns
Valve disease (yes/no)	7.8/7.9	ns	23.8/17.5	$p<0.05$
Pacemaker installed (yes/no)	6.9/8.0	ns	17.6/19.9	ns
Stroke (yes/no)	15.0/7.0	<0.01	23.6/19.2	ns
Peripheral vasculopathy (yes/no)	8.1/7.8	ns	26.0/18.9	ns
COPD (yes/no)	9.8/7.1	ns	21.0/19.2	ns
BMI (≤30/>30 kg/m^2)	9.5/5.2	<0.05	19.2/20.9	ns
Oedema (yes/no)	12.3/5.8	<0.001	26.1/15.1	<0.001
NYHA (I–II/III–IV)	7.6/9.0	ns	16.5/27.3	<0.001
Anaemia (yes/no)	12.4/6.5	<0.01	26.5/17.9	<0.01
GFR (≤60/>60 ml/min)	10.4/4.2	<0.001	20.1/19.9	ns
LVH (yes/no)	8.5/7.7	ns	23.6/18.4	ns
LVEF (<50%/≥50%)	8.9/5.7	ns	24.7/19.4	ns
Coronariography (yes/no)	7.0/8.1	ns	25.8/18.3	<0.05
Diuretics (yes/no)	8.3/5.8	ns	19.4/21.3	ns
ACEIs (yes/no)	8.7/7.2	ns	20.7/18.8	ns
ARAs (yes/no)	7.4/8.1	ns	20.6/19.3	ns
Beta-blockers (yes/no)	7.2/8.1	ns	17.0/20.7	ns
ACEI and/or ARA (yes/no)	8.3/6.8	ns	20.2/18.3	ns
ACEI and/or ARA+BB (yes/no)	7.1/8.1	ns	17.3/20.3	ns
Aldosterone antagonists (yes/no)	5.2/8.4	ns	21.6/19.3	ns
Digitalis (yes/no)	8.2/7.7	ns	18.9/20.2	ns
Calcium antagonists (yes/no)	10.0/7.4	ns	21.4/19.3	ns
Residence (Barbanza/others)	6.8/8.1	ns	14.2/20.9	<0.05

M/F, male/female; HT, arterial hypertension; COPD, chronic obstructive pulmonary disease; BMI, body mass index; NYHA, New York Heart Association functional class; GFR, glomerular filtration rate as given by the Cockcroft–Gault formula; LVH, left ventricular hypertrophy; LVEF, left ventricular ejection fraction; ACEI, angiotensin-converting enzyme inhibitor; ARA, angiotensin II receptor antagonist; BB, beta-blocker; ns, not statistically significant.

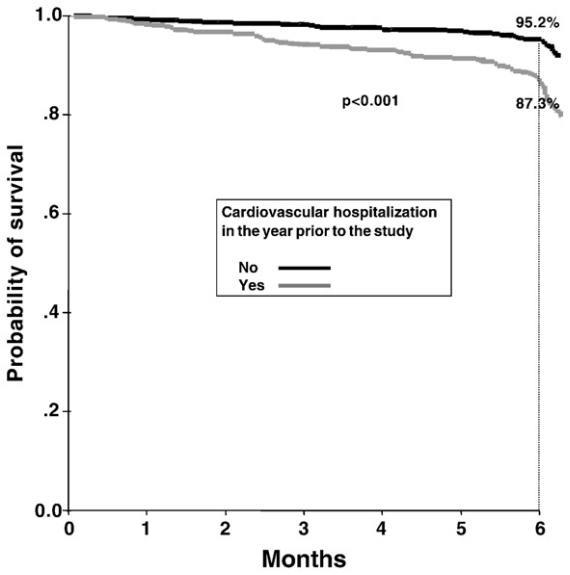

Fig. 1. Probability of survival free from re-hospitalization for cardiovascular reasons among GALICAP study patients who had or had not been hospitalized for cardiovascular reasons in the year prior to their inclusion in the study.

clinical practice guidelines' recommendations and a significantly higher use of beta-blockers (34% vs 25%; $p<0.01$) and ACEI (52% vs 47%; $p<0.05$).

The above risk factors have also been identified in several other recent studies [12,20,25,26]. We believe that particular importance should be given to ischaemic cardiopathy, anaemia, and depressed systolic function. The unfavourable prognosis of patients with HF of ischaemic origin suggests that all HF patients should undergo coronariography, and probably also myocardial viability tests, and should be revascularized if necessary. Anaemia is common among HF patients and is generally associated with greater severity, and there is evidence [27] that its correction might improve clinical status and prognosis (especially in the presence of kidney failure); the efficacy of routine treatment with iron and/or erythropoiesis stimulators is currently being evaluated in clinical trials [28]. The prognostic significance of depressed systolic function is currently under debate, association with poorer prognosis having been observed in some studies [22,29] but not others [20,25,30]; this uncertainty may derive partly from the influence of sample characteristics such as mean age and the prevalence of ischaemic cardiopathy, and partly from methodological discrepancies such as the treatment of LVEF as a continuous or a dichotomous variable.

It is striking that in this study the prescription of drugs of proven prognostic benefit, such as beta-blockers, only emerged as an independent predictor of more favourable outcome for patients younger than 70 years. The efficacy of these drugs has been observed not only in clinical trials (which as noted above have tended to use patients in a better-than-average overall condition), but also in community studies [12]. The causes of this discrepancy may include the advanced age of our subjects; the high proportion of patients with preserved systolic function (whose prognosis has not been shown to be improved by ACEIs, ARAs or beta-blockers); under-dosage; noncompliance; and the shortness of the follow-up period. On the other hand and accordingly to our results, the SENIORS trial, the first one that was focused on elderly population with HF and was undertaken to determine the effect of beta-blocker, nebivolol, on mortality and morbidity, regardless of ejection fraction, revealed that the benefits of this drug was less in patients >75 years. So, it is possible that beta-blockers or any other treatments are less effective in the very elderly patients [31].

4.1. Implications and limitations

We believe that the present study will have sampled practically the entire population of HF patients in the study area, and that it therefore portrays HF in this area more

Table 4
Results of Cox proportional hazards regression analyses for the combined outcome death and/or hospitalization for cardiovascular reasons in the whole sample and in subgroups defined by age or aetiology.

	Whole sample		Age				Aetiology			
			<70 years		≥70 years		Ischaemic		Non-ischaemic	
	HR	95%CI	HR	95%CI	HR	95%CI	HR	95%CI	HR	95%CI
Ischaemic	1.76	1.29–2.40			2.01	1.44–2.80				
Stroke	1.79	1.18–2.73			1.89	1.25–2.88	2.54	1.39–4.65		
Oedema	1.49	1.10–2.03								
Anaemia [a]	1.66	1.21–2.27	2.91	1.44–5.87	1.52	1.09–2.13			1.75	1.26–2.44
LVEF<50%	1.62	1.19–2.20			1.45	1.03–2.03	1.82	1.77–2.82		
Beta-blockers			0.42	0.20–0.89						
PCVH	2.33	1.67–3.24			2.26	1.59–3.20	2.99	1.82–4.91	2.01	1.46–2.78
Barbanza [b]	0.56	0.37–0.86			0.60	0.38–0.95				

HR, hazard ratio; CI, confidence interval; Ischaemic, ischaemic cardiopathy; LVEF, left ventricular ejection fraction; PCVH, hospitalization for cardiovascular reasons in the year prior to inclusion in the study.
Only factors identified as having independent influence on the outcome are listed.
[a] Anaemia was taken to be indicated by haemoglobin levels lower than 13 g/dl in men and 12 g/dl in women.
[b] Residence in the Barbanza district.

accurately than studies of currently hospitalized patients. Our criteria for inclusion in the study will have excluded any patients with HF who have never been hospitalized on account of this condition, but given the nature of HF we believe that the existence of any such patients in the study area is very unlikely. We have preferred to risk excluding this group rather than risk the inclusion of patients for whom the diagnosis of HF is doubtful, a practice that has probably distorted the results of a number of studies of HF. In the present study the probability of erroneous diagnosis must have been very small because all diagnoses were corroborated in hospital, even though they were only confirmed echocardiographically in 67% of cases.

4.2. Conclusions

The incidence of mortality and morbidity among Galician HF patients is high, though lower than in a number of other community studies. The dire consequences of HF for patients, and the cost of frequent re-hospitalizations for health services, point to a need to develop multidisciplinary HF care programmes that optimize the use of resources.

Acknowledgement

We thank Laboratorios Almirall SA for their unconditional collaboration in this study.

Appendix A. The GALICAP researchers

José Muñoz-Novoa, María Paseiro-García, Jesús Blanco-Montes, Victoria Bonome-González, Bernardo de Miguel-Bartolomé, Antonio Tenreiro-Varela, Ana Carvajal-de la Torre, Concepción Blanco-Sánchez, Margarita Palacios-Martínez, María Criado-Campomanes, Laura Calvo-Quintela, Antonino Caruncho-Conde, Cristina Iglesias-Díaz, María Veleiro-Tenreiro, Rogelio Seoane-Blanco, Tomás Benito-Martín, Luisa Allande-Menéndez, Jacobo Cadalso-Arrojo, Pilar Matas-Vázquez, Miguel Pedrosa-López, Carlos Prego-Rey, Manuel Tarrío-Tovar, Lucía Rodríguez-Cameselle, Julián Martínez-Montero, Carlos Piñeiro-Díaz, Baldomero Ríos, Eudaldo Sieiro-Prada, Gabriel Calvo-Mosquera, Jesús de Juan-Prego, María Grandal-Amor, Ignacio Cabezón-Lorenzo, María Castro-Ocampo, José López-Pérez, María Meijome-Sánchez, Jesús Illade-Cerdeiras, Santiago Torreira-Mouro, José López-Docasar, Juan López-Villasante, Ciriaco Varela-Rotger, Juan Caamaño-Mata, Ricardo Iglesias-Losada, Jacobo Laya-García, Luisa Zapata-Medín, María López-Varela, María Rodríguez-Solórzano, Serafín Bartolomé-Pérez, Francisco Pazos-Soto, José Pazos-López, Paula de Blas-Abad, Carmen Pastor-Benavent, María Juiz-Crespo, Victorino Turrado-Turrado, Ángel Lado-Llerena, Jaime Dopico-Pita, Miguel Pérez-Llamas, Leopoldo Vaamonde-Mosquera, Manuel Lado-López, Jerónimo Domínguez-López, José Gómez-Vázquez, Antonio Fernández-Seoane, Genaro Gutiérrez-Fernández, Rosa de la Fuente-Mariño, José Santos-Rodríguez, Ricardo Besada-Gesto, Rubén Blanco-Rodríguez, Vicente Parga-García, Germán Allut-Vidal, Javier Maestro-Saavedra, Concepción de Frutos-Marcos, Ramona Esteban-Álvarez, Rosa Liñares-Stolle, Ana Navaza-Dafonte, Pilar Rodríguez-Ledo, Inés Yeguas-Sánchez, Juan Latorre-Domínguez, Juan Fernández-Fernández, Clara Ares-Nistal, Rosa Carballal-González, Aurea Mejuto-Rodríguez, José Veiga-Gómez, Manuel López-Lens, Jerónimo Fernández-Torrente, Marcial Sanjurjo-Fernández, María Montero-Cabanas, José Pellit-Ramil, Mercedes González-Pérez, Aquilino Vázquez-Fernández, Francisco Angulo-Sánchez, Antonio Pedreira-Penedo, José Ramos-Sandiás, Manuel González-Rodríguez, Raimundo Gulín-González, María Sánchez-Cougil, Pilar Alonso-Álvarez, José Yáñez-Fernández, Juan Gago-Prada, Salvador Rey-Suárez, José Lamelas-García, Antonio González-Álvarez, Andrés García-Mata, Jorge Lloveres-Insua, Marta Michelena-Montes, Francisco Marcos-Fernández, Montserrat González-Teijeiro, José Vázquez-Vidal, José Araujo-López, Bernardo Viqueira-Pérez, Luis Germade-Fernández, Jesús Menduiña-Sanín, Francisco Becoña-de la Torre, Francisco Carrera-Guerreiro, César Romero-García, Carlos Andrade-Cochón, Constantino Simal-Garrido, Javier Álvarez-Rial, Gerardo Iglesias-Lobejón, Abilio Escribano-Ballestero, Rafael Cañadilla-Moraleda, José Quintana-Garrido, Alberto Pérez-Freijomil, Carlos Fandiño-Rivera, Andrés Santiago-Souto, Gerardo Miniño-Couto, Fernando Casal-Redondo, Lino Fontaiña-Pérez, Jesús Martínez-Barrios, José Moliner-de la Puente, Julia Bóveda-Fontán, José Martincano-Gómez, Antonio Fernández-Crespo, María Valiña-Miñones, Felisa Domínguez-Grandal, Pedro Callejas-Cabanillas, María Barros-Gutiérrez, Carlos Pérez-Pérez, Francisco Bacariza-Piñón, Francisco García-Soidán, Manuel Domínguez-Sardiña, Jacinto Mosquera-Nogueira, Manuel Nieto-Pereira, Teresa Ríos-Rey.

References

[1] Cleland JGF, Khand A, Clark AL. The heart failure epidemic: exactly how big is it? Eur Heart J 2001;22:623–6.
[2] Rodríguez-Artalejo F, Banegas Banegas JR, Guallar-Castillón P. Epidemiología de la insuficiencia cardíaca. Rev Esp Cardiol 2004;57:163–70.
[3] Vinson JM, Rich MW, Sperry JC, et al. Early readmission of elderly patients with congestive heart failure. J Am Geriatr Soc 1990;38:1290–5.
[4] Krumholz HM, Chen YT, Wang Y, et al. Predictors of readmission among elderly survivors of admission with heart failure. Am Heart J 2000;139:72–7.
[5] Galofré N, San Vicente L, González JA, et al. Morbimortalidad de los pacientes ingresados por insuficiencia cardíaca. Factores predictores de reingreso. Med Clin 2005;124:285–90.
[6] Atienza F, Anguita M, Martínez-Alzamora N, et al. Multicenter randomized trial of a comprehensive hospital discharge and outpatient heart failure management program. Eur J Heart Fail 2004;6:643–52.
[7] Duaso E, Díez-Caballero M, Formiga F. Abordaje de la insuficiencia cardíaca en ancianos: una visión desde la atención primaria. Rev Esp Cardiol 2006;59:290–1.
[8] Galbreath AD, Krasuski RA, Smith B, et al. Long-term healthcare and cost outcomes of disease management in a large, randomized, community-based population with heart failure. Circulation 2004;110:3518–26.
[9] Kimmelstiel C, Levine D, Perry K, et al. Randomized, controlled evaluation of short- and long-term benefits of heart failure disease

management within a diverse provider network: the SPAN-CHF trial. Circulation 2004;110:1450–5.
[10] Poole-Wilson PA, Swedberg K, Cleland JGF, et al. Comparison of carvedilol and metoprolol on clinical outcomes in patients with chronic heart failure in the Carvedilol Or Metoprolol European Trial (COMET): randomised controlled trial. Lancet 2003;362:7–13.
[11] Pfeffer MA, Swedberg K, Granger CB, et al. Effects of candesartan on mortality and morbidity in patients with chronic heart failure: the CHARM-Overall programme. Lancet 2003;362:759–66.
[12] Komajda M, Lapuerta P, Hermans N, et al. Adherence to guidelines is a predictor of outcome in chronic heart failure: the MAHLER survey. Eur Heart J 2005;26:1653–9.
[13] Permanyer Miralda G, Soriano N, Brotons C, et al. Características basales y determinantes de la evolución en pacientes ingresados por insuficiencia cardíaca en un hospital general. Rev Esp Cardiol 2002;55: 571–8.
[14] Varela Román A, González-Juanatey JR, Basante P, et al. Clinical characteristics and prognosis of hospitalised inpatients with heart failure and preserved or reduced left ventricular ejection fraction. Heart 2002;88:249–54.
[15] Lee DS, Austin PC, Rouleau JL, et al. Predicting mortality among patients hospitalized for heart failure: derivation and validation of a clinical model. JAMA 2003;290:2581–7.
[16] Otero-Raviña F, Grigorian-Shamagian L, Fransi L, et al. Estudio Gallego de Insuficiencia Cardíaca en Atención Primaria (Estudio GALICAP). Rev Esp Cardiol 2007;60:373–83.
[17] Cifkova R, Erdine S, Fagard R, et al. Practice guidelines for primary care physicians: 2003 ESH/ESC hypertension guidelines. J Hypertens 2003;21:1779–86.
[18] Zile MR, Baicu CF, Gaasch WH. Diastolic heart failure — abnormalities in active relaxation and passive stiffness of the left ventricle. N Engl J Med 2004;350:1953–9.
[19] Anguita Sanchez M. Investigadores del Registro BADAPIC. Características clínicas, tratamiento y morbimortalidad a corto plazo de pacientes con insuficiencia cardíaca controlados en consultas específicas de insuficiencia cardíaca. Resultados del Regiatro BADAPIC. Rev Esp Cardiol 2004;57:1159–69.
[20] Cleland JG, Swerberg K, Follath F, et al. The EuroHeart Failure Survey Programme — a survey on the quality of care among patients with heart failure in Europe. Part 1: patient characteristics and diagnosis. Eur Heart J 2003;24:442–63.
[21] Owan TE, Hodge DO, Herges RM, et al. Trends in prevalence and outcome of heart failure with preserved ejection fraction. N Engl J Med 2006;355:251–9.
[22] Solomon SD, Anavekar N, Skali H, et al. Influence of ejection fraction on cardiovascular outcomes in a broad spectrum of heart failure patients. Circulation 2005;112:3738–44.
[23] Pitt B, Remme W, Zannad F, et al. Eplerenone, a selective aldosterone blocker, in patients with left ventricular dysfunction after myocardial infarction. N Engl J Med 2003;348:1309–21.
[24] Granger BB, Swedberg K, Ekman I, et al. Adherence to candesartan and placebo and outcomes in chronic heart failure in the CHARM programme: double-blind, randomised, controlled clinical trial. Lancet 2005;366:2005–11.
[25] Varela-Román A, Grigorian-Shamagian L, Barge E, et al. Heart failure in patients with preserved and deteriorated left ventricular ejection fraction. Heart 2005;91:489–94.
[26] Grigorian Shamagian L, Varela Román A, García-Acuña JM, et al. Anaemia is associated with higher mortality among patients with heart failure with preserved systolic function. Heart 2006;92:780–4.
[27] Komajda M. Prevalence of anaemia in patients with chronic heart failure and their clinical characteristics. J Card Fail 2004;10:S1–4.
[28] Westenbrink BD, Visser FW, Voors AA, et al. Anaemia in chronic heart failure is not only related to impaired renal perfusion and blunted erythropoietin production, but to fluid retention as well. Eur Heart J 2007;28:166–71.
[29] Lenzen MJ, Scholte op Reimer WJ, Boersma E, et al. Differences between patients with a preserved and a depressed left ventricular function: a report from the EuroHeart Failure Survey. Eur Heart J 2004;25:1214–20.
[30] Bhatia RS, Tu JV, Lee DS, et al. Outcome of heart failure with preserved ejection fraction in a population-based study. N Engl J Med 2006;355: 260–9.
[31] Flather MD, Shibata MC, Coats AJ, et al. Randomized trial to determine the effect of nebivolol on mortality and cardiovascular hospital admission in elderly patients with heart failure (SENIORS). Eur Heart J 2005;26:215–25.