### Introduction and objectives

To assess baseline characteristics, management patterns, and clinical outcomes after 18 months in patients diagnosed as heart failure in a tertiary hospital in Catalonia, Spain.

### Methods

The records of all 265 patients admitted to the Hospital General Vall d’Hebron from July through December 1998 with a diagnosis of heart failure who met study criteria were identified and analyzed. Patients were interviewed by telephone 18 months later.

### Results

The mean age of the study population was 75 ± 12 years. 42% were male, 19% were admitted for causes other than heart failure, and 62% had significant comorbidity. Ventricular function was assessed in 68% (preferentially patients with a better prognosis), and was considered normal in 41%. Angiotensin-converting enzyme inhibitors or angiotensin II antagonists were used in 54%, and beta-blockers in 4%. The 18-month mortality was 46% (77% cardiac mortality). Multivariate predictors of death were older age, severe or previous heart failure, and serious comorbidity. At 18 months, 69% of survivors were in functional classes I or II.

### Conclusions

1) As in other geographic areas, patients in this study were an older population with poor survival; 2) local patterns of care definitely need improvement; 3) comorbidity is important for pronosis, and 4) a significant proportion of survivors enjoy an acceptable quality of life long after discharge.

### Key words: Heart failure. Prognosis. Survival.

### See Editorial on Pages 563-4

Study financed by grant 12/15/98 of the Agència d’Avaluació de Tecnologia Mèdica.

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Received 12 April 2001. Accepted for publication 19 February 2002.

### INTRODUCTION

Knowledge of the characteristics and outcome of the patients seen in daily clinical practice who differ from those included in clinical trials in major ways is a key aspect of the treatment of heart failure. Although important findings have been reported recently,¹ ¹¹ information relative to the demographic and clinical...
characteristics, medical action, patient preferences and outcome of heart failure in unselected populations in many countries, including western ones, is still insufficient. The need for this type of information has been widely recognized.14,15

The present study was designed to ascertain the baseline characteristics, patterns of treatment, and clinical results of patients diagnosed as heart failure admitted to a tertiary general hospital in Catalonia. In Spain, some general epidemiological data on heart failure are known, basically in relation to morbidity, mortality and baseline characteristics in the hospitalized population.16-22 Nevertheless, more precise knowledge of the specific clinical characteristics and long-term outcome of the disease, as well as the patterns of treatment in daily practice, is needed. This knowledge would allow specific aspects of care that can be improved to be identified and acted on.

METHODS

All the patients hospitalized in the Hospital General Vall d’Hebron who were diagnosed of heart failure from 1 July to 31 December 1998 were selected for the study. The Hospital General Vall d’Hebron is a tertiary teaching hospital in which many admissions take place from the emergency room, since the hospital also serves as a secondary hospital for an urban community of approximately 450 000 inhabitants. The exclusion criteria were heart failure secondary to a reversible intercurrent cause in patients with no other finding indicative of previous heart failure, chronic cor pulmonale, terminal concomitant disease, and foreign patients for which no follow-up was available.

All the patients admitted to the hospital between 1 July and 31 December 1998 in which heart failure was listed as the first or second diagnosis at discharge (ICD-9 codes 428.0, 428.1, and 428.) were identified from the admission list. The corresponding clinical histories, including chest radiographs, electrocardiograms, and echocardiogram reports were reviewed by the investigative team. The patient was not included if he or she met exclusion criteria or if the investigative team considered that the diagnosis of heart failure issued was not sufficiently documented according to the Framingham criteria.8 The data corresponding to the hospital stay were collected by the investigators from a detailed review of each clinical history and recorded in a computer database prepared expressly for the study. A physician of the investigative team carried out a structured telephone interview at a mean of 18 months after hospital discharge. When the patient was not initially located, attempts were repeated later. The interview included questions relative to the functional class of the New York Heart Association (NYHA) classification, daily life activities and, in patients who died after discharge, the date and probable cause of death. The clinical histories of the patients who died after release were reviewed to assess the cause of death, in case it occurred during a readmission.

Statistical analysis

Categorical variables were compared by means of the Chi-square statistical test. Multivariate analysis for the prediction of death was carried out using the Cox model of proportional risks, which included all the variables that were significant in previous bivariant analysis, or in the analysis made with the Kaplan-Meier method (to a level of 0.05), or considered necessary to adjust the model correctly (such as, for example, sex, age, previous heart failure, systolic function, hypertensive heart failure, previous cardiac valve diseases, or place of admission). The risk ratios were calculated from the coefficients and 95% confidence intervals (CI) were established for significant variables. Kaplan-Meier survival curves were constructed for mortality, comparing patients older and younger than 75 years with other subgroups. A model of logistic regression was prepared to predict reaching functional class III-IV or death at the end of the follow-up, including the variables that were statistically significant in bivariant analysis of mortality and the variables that were considered clinically important like sex, age, place of admission, diabetes, smoking, other diseases, or systolic function. The odds ratio and 95% CI were calculated for significant variables.

RESULTS

Of the 324 patients who were selected for the study, 18% met exclusion criteria or had a diagnosis of heart failure that was considered insufficiently documented. Finally, the remaining 265 patients were included, constituting the population of the present study.

Baseline characteristics

In Table 1 are presented the main demographic and clinical characteristics of the population, emphasizing a high rate of comorbidity (62%), defined as kidney failure (serum creatinine >2 mg/dL), malignant neoplasm, peripheral arteriopathy, cerebrovascular disease, and other serious neurological diseases documen-
In Figure 1 is shown the distribution of ages by decades. As can be observed, almost 40% of the patients were over 80 years old, and more than 70% were over 70 years of age. In Table 1 are shown other notable characteristics of the study population, such as a high proportion of patients in functional class III-IV (88%), with clinically acute pulmonary edema (26%), the high proportion of patients (19%) hospitalized for causes other than heart failure (basically pneumonia, other non-cardiac infections, surgery, or neoplasm). The patients over 75 years old were mainly women (67%) and often hospitalized in the Internal Medicine Service (63%), but showed no other relevant baseline differences. Table 2 shows that the immense majority (96%) of the patients hospitalized for heart failure were in an advanced functional class. Nonetheless, a large proportion (60%) of the patients hospitalized for other causes with concomitant heart failure were also in an advanced functional class. The possible causal factors of heart failure that were identified (not mutually exclusive) in the discharge report and review of the clinical histories were arterial hypertension in 50%, coronary artery disease in 35%, cardiac valve disease (operated or not) in 24%, cardiomyopathy in 6%, and others in 3%. No possible causal factors were identified in 13% of the patients.

The systolic function was considered normal in 41% of the patients in which it was studied (68.3% of the total population; see below), and it was judged as mild or moderately depressed in 36% and severely depressed in 23%. Among the patients whose systolic function was considered normal, there was a significantly greater proportion of hypertensive patients and a significantly smaller proportion of patients with coronary artery disease than among those whose systolic function was considered depressed (64% versus 49% and 24% versus 54%, respectively). There was a greater proportion of patients in atrial fibrillation among them.

**Patterns of management**

Only 21% of the patients were hospitalized in the cardiology department; 56% were hospitalized in the internal medicine department, and 23% in other areas of the hospital (in most of these patients the cause of admission was not heart failure). The patients over 75 years for the most part were women (67%) and were hospitalized more often in the internal medicine department (63%). There were no other relevant baseline differences. The mean ages of these three subgroups, according to the department where they were admitted, were 70, 77 and 76 years, respectively. Ventricular function was assessed in 68.3% of patients (mostly by

| TABLE 1. Clinical and demographic characteristics of the study population (n=265) |
|---------------------------------|-----------------|----------------|
| Age (years)                     | Mean            | SD             |
| Mean                             | 75              | 12.33          |
| **n (%)**                       |                 |                |
| Men                              | 113 (43)        |                |
| History of heart failure         | 183 (69.1)      |                |
| Reason for admission            |                 |                |
| Heart failure                    | 195 (73.5)      |                |
| Acute myocardial infarction      | 20 (7.5)        |                |
| Others*                          | 50 (19)         |                |
| NYHA functional class**          |                 |                |
| I                               | 6 (2.7)         |                |
| II                              | 26 (9.85)       |                |
| III                             | 88 (33.33)      |                |
| IV                              | 144 (54.5)      |                |
| Pulmonary edema                  | 70 (26.4)       |                |
| Biventricular heart failure      | 155 (58.5)      |                |
| Diabetes mellitus                | 92 (34.7)       |                |
| Other previous diseases***       | 164 (61.9)      |                |
| Atrial fibrillation              | 118 (45.7)      |                |

| *Includes mainly pneumonia and other non-cardiac infections, surgery, or neoplasm. **Patients with acute myocardial infarction. Killip 2 were assigned conventionally to NYHA functional class I, and Killip 3 and 4 patients to functional class IV. ***Includes kidney failure, neoplasm, peripheral arteriopathy, or cerebrovascular disease and other neurological diseases.

| TABLE 2. New York Heart Association functional class in relation to reason for admission (excluding myocardial infarction) |
|-------------------------------------------------|-----------------|-----------------|
|        | I (%) | II (%) | III (%) | IV (%) |
| Heart failure                                  | 1 (0.5) | 7 (4) | 67 (34.5) | 119 (61) |
| Others                                         | 5 (10) | 15 (30) | 20 (40) | 10 (20) |
| Overall                                        | 6 (2) | 22 (9) | 87 (36) | 129 (53) |

*Includes mainly pneumonia and other non-cardiac infections, surgery, or neoplasm. **Patients with acute myocardial infarction. Killip 2 were assigned conventionally to NYHA functional class I, and Killip 3 and 4 patients to functional class IV. ***Includes kidney failure, neoplasm, peripheral arteriopathy, or cerebrovascular disease and other neurological diseases.
Echocardiogram, but also by contrast or radionuclide ventriculography) during admission or in the 3 preceding months. Ventricular function was assessed in 92.6% of the patients under 75 years versus 60.5% of the patients over 75 (P<.005), in 90.9% of the patients admitted to the cardiology department (where younger and male patients also predominated) versus 62.4% of patients admitted to other wards (P<.005). The proportion of patients with normal or impaired ventricular function did not vary with age.

Altogether, angiotensin-converting enzyme inhibitors (ACEI) or angiotensin II antagonists (ARA II) were administered during admission or prescribed at release to 54% of the patients. Digoxin was prescribed for 38.3%, diuretics for 93.15%, and beta-blockers (carvedilol or others) for 4%. ACEI or ARA II were used in 61.3% of the patients in which ventricular function had been studied, in 38.75% of those in which it was not studied (P<.005), and in 72.2% of those in which ventricular function was judged to be impaired versus 46.5% of those in which it was considered normal. There were no significant differences in the rates of ACEI or ARA II use between patients 75 years old or older and those younger than 75 (52% versus 56.9%, respectively).

**Clinical results**

The mean hospital stay was 9.1 days and 38.5% of the survivors required readmission or emergency care. The mortality during admission was 6.4%. After discharge, 8% of the patients were lost to follow-up, but there was no difference in the baseline characteristics of these patients and those who could be contacted at the end of follow-up. One hundred twenty-two patients died in the course of the study, so the total mortality between admission and the follow-up interview was 18 months (a mean of 498±206 days in survivors) was 46%. In the patients who were lost to follow-up, the duration of the hospital stay and its contribution to the total follow-up time was considered. The physician who carried out the interview judged that the cause of death was of cardiac origin in 76.8% of cases and non-cardiac in 23.2% (in the 12 patients that died during hospital readmission, death was due to a cardiac cause in 5 and a non-cardiac cause in 7). The main causes of non-cardiac death were neoplasms, cerebrovascular accidents, and kidney failure. Among the patients who died, death was considered to have a cardiac origin in 80% of those admitted for heart failure, in 100% of those hospitalized for myocardial infarction, and in 52.6% of those hospitalized for other reasons. The mean age of the patients who died was 79.6 years versus 71.7 years in survivors. The impact of age on mortality is illustrated in Figure 2, and it can be seen that the survival of patients 75 years and older was significantly lower than that of younger patients. Bivariate comparisons to assess the determinants of mortality are shown in Table 3. It can be observed how age, the severity of the disease according to functional class, and the presence of biventricular heart failure were associated with a greater mortality. It is noteworthy that ventricular function was studied more often in the patients with a better prognosis. Overall mortality was greater in patients in whom ventricular function was not studied by any method (a group that included a larger proportion of older persons and patients hospitalized for causes other than heart failure). In this group, 70% of the deaths were of cardiovascular origin, versus 81% in the patients who underwent a study of ventricular function (non-significant difference). Sex and normal ventricular function (when studied) were not associated with a significantly different mortality rate, nor was admission for causes other than heart failure. Likewise, no single cause seemed to have an especially worse vital prognosis than the rest. For example, survival did not differ in patients with and without manifestations of coronary heart disease (documented myocardial infarction or demonstration of myocardial ischemia or coronary stenosis). In the multivariate analysis, independent predictors of death (Table 4) were age over 75 years, biventricular heart failure, and comorbidity. Systolic function was not predictive of mortality, whether it was included in the analysis as normal, depressed, or not studied, or even (in two analyses not shown) assuming extreme cases in which the patients whose ventricular function was not studied had either normal or impaired ventricular function. In the patients who survived until discharge, the same predictors of delayed mortality were observed (data not presented). At the time of the follow-up interview, 68.6% of the survivors were functional class I-II as determined by direct assessment of the intervie-
TABLA 3. Overall mortality rates in relation to clinical variables (bivariant analysis)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes n (%)</td>
</tr>
<tr>
<td>Sex: women</td>
<td>71 (58.2)</td>
</tr>
<tr>
<td>Age: ≥75 years</td>
<td>91 (74.6)</td>
</tr>
<tr>
<td>FC at admission: III-IV</td>
<td>115 (94.3)</td>
</tr>
<tr>
<td>Reason for admission: HF-AMI</td>
<td>102 (83.6)</td>
</tr>
<tr>
<td>Biventricular HF</td>
<td>89 (72.9)</td>
</tr>
<tr>
<td>History of HF</td>
<td>93 (76.2)</td>
</tr>
<tr>
<td>Other previous diseases</td>
<td>86 (70.5)</td>
</tr>
<tr>
<td>Ventricular function studied</td>
<td>72 (59)</td>
</tr>
<tr>
<td>Impaired systolic function</td>
<td>44 (61.1)</td>
</tr>
</tbody>
</table>

FC indicates functional class of the New York Heart Association; AMI, acute myocardial infarction; HF, heart failure.

TABLA 4. Multivariate predictors of death at 18 months (Cox proportional risks model)

<table>
<thead>
<tr>
<th>Predictor</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age ≥75 years</td>
<td>3.05</td>
<td>(1.94-4.79)</td>
</tr>
<tr>
<td>Biventricular heart failure</td>
<td>2.19</td>
<td>(1.44-3.33)</td>
</tr>
<tr>
<td>History of heart failure</td>
<td>1.58</td>
<td>(0.99-2.50)</td>
</tr>
<tr>
<td>Other previous diseases</td>
<td>1.94</td>
<td>(1.25-2.99)</td>
</tr>
</tbody>
</table>

OR indicates odds ratio; CI, confidence interval.

TABLA 5. Multivariate baseline predictors of functional class III-IV or death at 18 months in contrast with survival in class I-II (multiple logistic regression analysis)

<table>
<thead>
<tr>
<th>Predictor</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age ≥75 years</td>
<td>5.83</td>
<td>(2.95-11.53)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>3.43</td>
<td>(1.61-7.32)</td>
</tr>
<tr>
<td>Comorbidity</td>
<td>2.55</td>
<td>(1.31-4.96)</td>
</tr>
<tr>
<td>Biventricular heart failure</td>
<td>2.21</td>
<td>(1.13-4.31)</td>
</tr>
<tr>
<td>History of heart failure</td>
<td>2.07</td>
<td>(1.01-4.28)</td>
</tr>
<tr>
<td>AF</td>
<td>1.98</td>
<td>(0.94-4.19)</td>
</tr>
</tbody>
</table>

CI indicates confidence interval; OR, odds ratio; AF, atrial fibrillation.

DISCUSSION

Epidemiological studies of heart failure have disclosed two important findings: in first place, heart failure is a syndrome that is increasingly predominant in persons of advanced age and, secondly, its mortality is high, much more than is observed in the selected populations of clinical trials. These two findings have been confirmed by several studies,7-11,13,23-27 although they have been made in geographically limited communities and have not always been population-based studies. On the other hand, information about certain clinical questions (such as the prevalence and meaning of normal systolic function or the influence of comorbidity on prognosis) or the outcome of the disease, aside from survival, is still scant. Also, relatively little is known about patterns of management in daily clinical practice. Increasing such knowledge in diverse geographic areas should be useful, among other reasons, in better understanding the applicability and possible impact of the treatments studied in clinical trials, whose population is clearly different. The present study, which is based on a carefully collected general hospital population of urban origin, helps to fill in some of the gaps mentioned in the Spanish panorama. It emphasizes, in first place, that the results observed in our population, such as the age (in both sexes) and short-term survival, are very similar to the figures reported in the McIntyre et al study based on more than 66,000 patients, who were also identified from hospital admissions. The area of origin of this study, Scotland, could possibly have a different profile of atherosclerosis risk factors, as observed in the MONICA study,28 which revealed that Scotland has one of the two highest rates of incidence of myocardial infarction, whereas the region of Spain where the present study was made (Catalonia) has one of the two lowest rates.29 We could ask if the different rates of coronary disease in the two zones could determine different patterns of etiology, age and survival in patients with heart failure, considering that the age of the patients differed in these studies (being younger in the population of the MONICA study). Apparently, this is not the case. Increasing prevalence with age and the high mortality rate, as observed in our study, are almost universal findings except in clinical trials. In other studies made in Spain,18,22 baseline characteristics of the study populations are comparable to those found in our study and in other countries. It is reasonable to assume that in studies, like ours, that are based on a hospital population reflect the worse extreme of the prognostic spectrum. For example, in the recent population-based Rotterdam study,13 a clearly lower mortality is reported but this does not occur in all studies.8,9,17,25 This question is still incompletely understood.
The predictors of mortality observed in our study do not differ substantially from those of other studies, in which age is also usually accompanied by clinical severity.\textsuperscript{8,30} In fact, the low proportion of patients initially in functional classes I and II who were included in our study suggests that our findings cannot be used to better characterize prognosis in such patients, which ideally should be assessed in population-based or primary care studies. It is noteworthy that these simple markers had a greater prognostic weight than more sophisticated indicators, like the existence of impaired ventricular function or coronary heart disease, in our study. Although it would have required a larger study population to establish this point more solidly (because this would have allowed the study of a larger number of patients with impaired ventricular function), and perhaps even another study design, the finding that normal systolic function is less important for prognosis than age or clinical severity is consistent with the findings of other studies.\textsuperscript{11,32} The importance of comorbidity in the evolution and prognosis of heart failure has only been addressed partially in the literature.\textsuperscript{7,30} Our study contributes data of interest on this topic, suggesting that concomitant diseases are frequent in patients with heart failure and have prognostic significance. Aside from observing a significant comorbidity in more than 60% of the patients, our study illustrates this interrelation in three different ways. In the first place, approximately 20% of the patients hospitalized for heart failure died of non-cardiac causes; secondly, comorbidity was an independent predictor of death and, finally, approximately half of the patients hospitalized for non-cardiac diseases died from cardiac causes, the overall mortality rate for this cause being similar to that of patients hospitalized for heart failure. Some of these findings must be interpreted with caution because they were obtained in telephone interviews. On the other hand, some of the causes of death that are considered non-cardiac, like stroke, could be a complication of heart disease. Nonetheless, in a high proportion of the patients in the small subgroup who died during a hospital readmission, death was not due to a cardiac cause. Therefore, our results suggest that the prognostic role of comorbidity should be better evaluated in future studies and, in addition, should be considered when the possible effect of therapeutic interventions is assessed in daily clinical practice.

With respect to management patterns, it is not surprising that only a small minority of patients will be hospitalized in the cardiology department, as a result of hospital logistics and some clinical characteristics of the population, like a high rate of comorbidity. This finding illustrates to what extent the management of heart failure surpasses the possibilities of present cardiological practice to become a more general problem, a topic that has been examined more thoroughly in the recent OSCUR study.\textsuperscript{12} As has been observed in other studies,\textsuperscript{12,13,33-35} ventricular function was not studied in more than one-fourth of the patients. It is interesting to confirm that in older patients and women this study was made with less assiduity than in younger patients and men, which makes it difficult to better characterize these subgroups. In fact, the subgroup of patients in which ventricular function was not studied had a significantly greater mortality than the group of patients in which it was studied. In addition, death was due to a cardiovascular cause in 70% of the patients who died. These findings may be related to the greater availability of studies of ventricular function in cardiology departments (where patient who are younger and have a better overall prognosis also usually predominate) and to different patterns of action in different specialties.\textsuperscript{12} In any case, it illustrates the tendency observed in other diseases towards the concentration of better care in patients with a better prognosis.\textsuperscript{33,34,36,37} The rate of ACEI or ARA II use during admission was lower than in other studies,\textsuperscript{6,12,35,38} but it is difficult to make direct comparisons. This low rate of use may reflect skepticism regarding the value of these drugs in elderly and ill patients (although the rates of use did not different in patients older and younger than 75 years), or doubts relative to their usefulness in the presence of normal systolic function. Nonetheless, our findings reveal an incongruity in medical conduct. While it is evident that the finding of impaired systolic function influenced the decision to give ACEI or ARA II, ventricular function was not assessed in 30% of the patients. The rate of beta-blocker use was very low. In addition to these possible reasons mentioned for ACEI or ARA II, in the period of our study some trials like CIBIS II had not yet been published, although bibliographic findings for carvedilol were available. On the other hand, 55% of the patients were in functional class IV, which then was considered an absolute contraindication for the use of beta-blockers. The reluctance of many doctors to use beta-blockers in other well-established indications has been clearly documented.\textsuperscript{39} Overall, the patterns of treatment in this population suggest that there is still room for improvement. Nonetheless, it seems legitimate to ask to what extent better compliance with recommendations based on scientific evidence would have improved the survival or quality of life of this group of patients, in which octogenarians with severe heart failure and serious associate diseases predominated. The median gain of only 4-5 months in the survival of the study population of McIntyre et al.\textsuperscript{7} observed in a period in which significant therapeutic advances had been made, explains why there is a certain degree of skepticism about the overall population.

Perhaps it is not surprising that more than half of the survivors had an acceptable functional situation 18
months after discharge, with 76.4% walking daily outside their homes and 24.8% stating that they had some recreational physical activity. However, a formal evaluation of the quality of life would certainly be needed to clarify this point and a longer follow-up time is required to detect more deterioration. The frequency with which functional class is acceptable seems particularly rewarding in an elderly population that has survived such a lethal disease. As could be expected, older patients not only die more, but are also in clinically poorer condition in the follow-up visit, whereas younger and healthier patients achieve a better clinical state.

Limitations of the study

The most important limitation of the present study is the limitation inherent to all retrospective reviews of patient populations diagnosed of heart failure, that is to say, difficulties in the clinical diagnosis of the condition. These difficulties have fueled demand for studies of ventricular function in clinical practice guidelines. Nonetheless, one of the reasons for interest in studies like this one and others in the literature is to confirm in what small measure these recommendations are followed in clinical practice, even in cases in which, as in our study, the meticulous review made of the clinical histories means that it is very likely that the diagnoses were correct. Evidently, this entails accepting that there may be a proportion of false positive diagnoses (and that undiagnosed patients may not be included). In addition to being a limitation of the study, it certainly is a shortcoming of clinical practice. In any case, in our study the outcome overall and in different subgroups is consistent with a generally correct diagnosis. On the other hand, in our area the data obtained in our study corroborate the main findings of more extensive studies. Other limitations of our study are its relatively small sample and local character, in addition to its dubious applicability to extrahospital patients.

CONCLUSIONS

Patients hospitalized with a diagnosis of heart failure correspond to a generally elderly population in serious condition with a poor prognosis. These demographic and mortality findings coincide with those observed in distant places. Our study also shows that there is much room for improvement in local therapeutic practice. In addition, it shows the importance of comorbidity and the scant relevance of normal systolic function in the prognosis. It also suggests that a significant proportion of the survivors enjoy an acceptable functional status more than one year after discharge. All these considerations are useful in designing a good therapeutic strategy in heart failure.

REFERENCES


