

Advances in the Management of Heart Failure (I)

Epidemiology of Heart Failure

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Approximately 1% of all persons over 40 years of age suffer heart failure. The prevalence of this disease doubles with each decade of life, reaching around 10% in persons over 70 years of age. In Spain, heart failure is responsible for nearly 80 000 hospital admissions every year—some 5% of all admissions. As in other developed countries, it is the most common cause of hospitalization among persons 65 years of age and over. The incidence of heart failure increases with age, and reaches 1% per year in those over 65. Heart failure is a progressive, lethal disorder, even with adequate treatment. Five year survival is around 50%—no better than that for many cancers. In Spain, heart failure is the third leading cause of cardiovascular mortality, after coronary heart disease and stroke. In 2000, heart failure caused 4% of all deaths and 10% of cardiovascular deaths among men; the corresponding figures for women were even higher at 8% and 18%. In recent decades, the prevalence and number of hospitalizations due to heart failure have increased steadily in developed countries. Heart failure will probably continue to increase in frequency in the coming years since there has been no appreciable reduction in its incidence. However, survival is increasing due to better treatment. The control of risk factors for hypertension and ischemic heart disease, the main causes of heart failure in Spain, is the only way to halt the foreseeable increase in the frequency of heart failure in the near future.

Key words: *Epidemiology. Heart failure. Spain.*

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Epidemiología de la insuficiencia cardíaca

Cerca del 1% de la población mayor de 40 años presenta insuficiencia cardíaca. La prevalencia de esta enfermedad se dobla con cada década de edad y se sitúa alrededor del 10% en los mayores de 70 años. En España se producen cerca de 80.000 ingresos hospitalarios por insuficiencia cardíaca cada año. Al igual que en otros países desarrollados, la insuficiencia cardíaca es la primera causa de hospitalización en mayores de 65 años y da cuenta, aproximadamente, del 5% de todas las hospitalizaciones. Se trata de una afección que aumenta con la edad y alcanza el 1% al año en los sujetos mayores de 65 años. La insuficiencia cardíaca es un trastorno progresivo y letal, aun con tratamiento adecuado. La supervivencia es de alrededor del 50% a los 5 años del diagnóstico, por lo que no es mejor que la de muchos cánceres. La insuficiencia cardíaca es la tercera causa de muerte cardiovascular en España, por detrás de la cardiopatía isquémica y la enfermedad cerebrovascular. En el año 2000, entre los varones, la insuficiencia cardíaca fue responsable del 4% de todas las defunciones y del 10% de todas las muertes por enfermedades cardiovasculares; entre las mujeres, los porcentajes correspondientes fueron del 8 y del 18%. En las últimas décadas, la prevalencia y las hospitalizaciones por insuficiencia cardíaca han aumentado de manera considerable en los países desarrollados. Se espera que su frecuencia siga creciendo en los próximos años, dado que no se han producido descensos apreciables en su incidencia; sin embargo, su supervivencia está mejorando gracias a la disponibilidad de mejores tratamientos. El control de los factores de riesgo, como la hipertensión y la cardiopatía isquémica, las principales causas de insuficiencia cardíaca en España, es el único medio para controlar el previsible aumento de esta enfermedad en el futuro.

Palabras clave: *Epidemiología. Insuficiencia cardíaca. España.*

INTRODUCTION

This article examines the frequency and distribution of heart failure and describes its determining factors in developed countries, with special reference to Spain.

Accurate knowledge of the epidemiology of a disease depends on good diagnostic criteria.^{1,2} Heart failure

is a clinical (and therefore symptomatic) syndrome frequently accompanied by symptomatic or asymptomatic left ventricular dysfunction. In early studies on the extent of heart failure, relatively non-specific clinical criteria were used, such as dyspnea, fatigue and edema. They therefore underestimated the problem of ventricular dysfunction (which is detected by echocardiography) and included subjects with symptoms of heart failure caused by other diseases.³

Knowing the frequency and prognosis of both systolic and diastolic heart failure and asymptomatic ventricular dysfunction is of interest. Unfortunately, there have been relatively few studies on diastolic heart failure due to a lack of clear diagnostic criteria. Although new criteria have been recently proposed,^{4,5} they have not been sufficiently used in epidemiological studies. The appearance of these new criteria was followed by a daring proposal to abandon the classification of heart failure based on the use of the ejection fraction as an indicator of systolic ventricular function.⁶

The lack of good diagnostic criteria for heart failure, and until relatively recently of effective treatment, has meant that our knowledge of its epidemiology has been poorer than that regarding other cardiovascular problems such as coronary heart disease or cerebrovascular disease. In Spain, only data for prevalence, hospital admissions and mortality are available. The remaining data of epidemiological interest have been extrapolated from the international (mainly Anglo-Saxon) literature.

PREVALENCE OF HEART FAILURE

The frequency of a disease is generally characterized by its prevalence and incidence. Prevalence refers to the number of cases of the disease occurring in a population within a specific time frame. It therefore provides information on the number of patients that require medical attention. The prevalence of a disease is usually determined from cross-sectional studies of the population; these are often undertaken with patients visiting medical centers. However, these studies normally underestimate the prevalence of the disease among the general population since not all patients visit their doctor, and it is quite normal for patients to present with an already serious or advanced condition. Population-based prevalence studies require important economic outlays; the more difficult it is to reach the population in question and the more expensive the tests required, the greater this outlay will be. Such studies do not usually involve the entire population of a country, except when the information required can be obtained by a questionnaire. Instead, they usually involve relatively small geographical regions, and the results are extrapolated to the national level. Care must be taken when com-

paring heart failure prevalence studies involving different regions since the diagnostic procedures used can be different. The age groups involved in different studies can also vary, and since the prevalence of heart failure increases with age, the direct comparison of results may not be possible.⁷

To our knowledge, only one study on the prevalence of heart failure has been performed in Spain,⁸ and its results are comparable to those reported in the literature. Approximately 1% of the general population aged 40 years or above suffers heart failure, and a further 2% show compatible signs and symptoms (although the latter can only be detected after a rigorous clinical examination and could be due to respiratory or renal problems).⁹ The prevalence of heart failure doubles with each consecutive decade and reaches about 10% in those over 70.^{8,9} In fact, the majority of patients presenting with heart failure are elderly. This is to be expected, not just because of the increased frequency of the problem but also because heart failure is less symptomatic in younger people.

Over recent decades, the prevalence of heart failure has been on the increase in developed countries.⁷ Several factors are responsible for this. Firstly, the number of elderly people (in whom the problem is more common) has increased, and secondly the number of people surviving acute myocardial infarction and high blood pressure (the two main causes of heart failure) is now greater due to improvements in treatment. This greater survival means patients eventually develop heart failure (a common feature of many cardiac diseases), which is therefore seen to be more common. In some ways, heart failure is the result of the chronic phase of acute myocardial infarctions or the complications of hypertensive heart disease owed to advances—but not cure—in medicine. Finally, there is evidence that the best heart failure treatments (mainly angiotensin converting enzyme inhibitors [ACE inhibitors] and beta-blockers) are beginning to increase survival rates.¹⁰ The greater the survival rate, the greater the prevalence of heart failure will be.

HOSPITAL ADMISSIONS DUE TO HEART FAILURE

Heart failure prevalence data can be complemented by the number of hospital admissions due to the disease—a figure that provides an idea of the associated healthcare burden. This information is interesting for several reasons. Firstly, the majority of countries keep systematic records on both private and public hospital admissions, and data are usually available at the national level. It is therefore a relatively cheap way of monitoring the problem. Secondly, the majority of healthcare costs associated with heart failure are generated by hospitalization. Thirdly, in its ad-

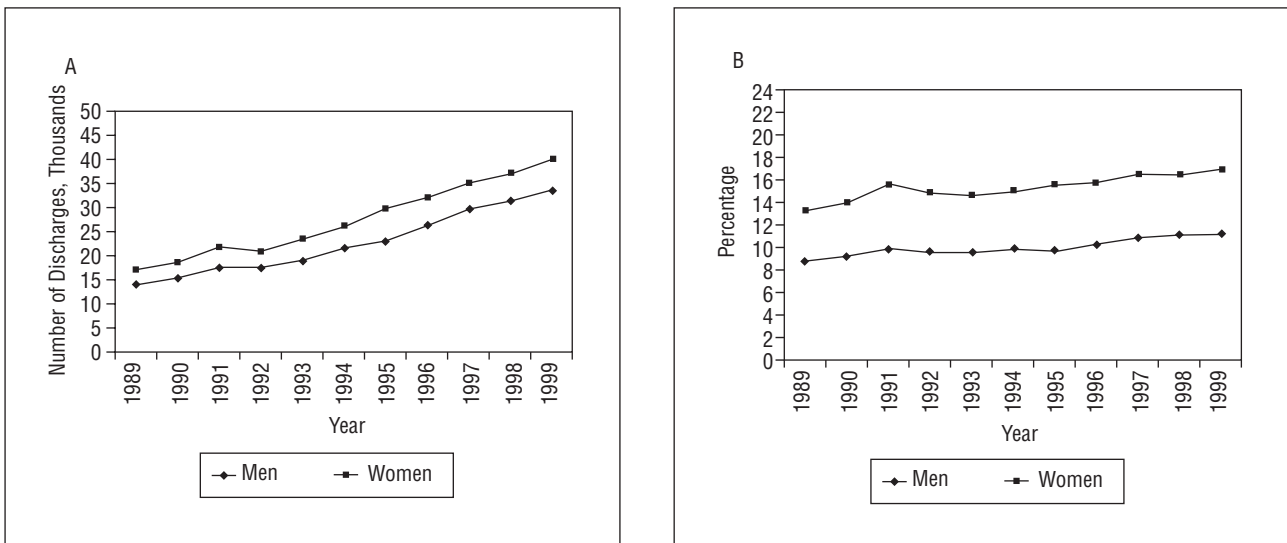


Fig. 1. A: number of hospital discharges of patients admitted with heart failure. B: admissions due to heart failure as a percentage of all-cause admissions in Spain (1989-1999). Code 228 of ICD-9 for the entire study period.

vanced stages, heart failure leads to repeated hospitalization. Nevertheless, it should be remembered that while the number of hospitalizations may provide adequate information on the healthcare burden, it does not necessarily do so with respect to the frequency of heart failure. The majority of health information systems do not provide data on the number of patients *per se*, but on the number of hospitalizations in a more administrative sense, i.e., they do not distinguish between first and second admissions etc. of the same patient. Further, the number of hospitalizations does not depend on the frequency of heart failure alone, but also on the availability of hospital beds and the admission policies of each hospital or health system. Geographical variability with respect to the number of hospital admissions for heart failure in Spain is in part due to the differences in hospital resources between provinces.¹¹

Some 80 000 hospital admissions for heart disease occur every year in Spain (Figure 1). As in other developed countries, heart failure is the number one cause of hospitalization in people over 65 years of age, followed by heart disease and ictus. Indeed, heart failure accounts for approximately 5% of all admissions.^{12,13} There is a clear seasonal pattern, with many more admissions occurring in winter than in summer.¹⁴ In addition, the number of admissions for heart failure has increased greatly in Spain in recent years (Figure 1), as in the majority of developed countries, and is likely to continue increasing in the immediate future due to the ageing of the population.^{7,12} In Spain, admission to hospital for this reason is more common among women than men (Figure 1A), and is increasing as a percentage of all admissions due to cardiovascular disease (Figure 1B).

INCIDENCE OF HEART FAILURE

Incidence measures the number of new cases of a disease over a given time period and provides information on the importance of the different risk factors in the general population. To measure disease incidence, people who are originally free of disease need to be monitored over the set time period and the number of new cases recorded. These studies are more informative when they are population-based and record both intrahospital and extrahospital cases. The most detailed data available on the incidence of heart failure are those provided by the Framingham study. Incidence increases with age, reaching 1% per year among people over 65 years of age. It is twice as high among hypertensive than normotensive subjects, and five times greater among those who have suffered a myocardial infarction than among those who have not.¹⁵

There have been very few studies that have recorded changes in the incidence of heart failure, mainly because a standard measuring system needs to be used over the entire period examined. In this respect, the Framingham study is again that which provides the best data. The incidence of heart disease has been stable among men since the 1950s, whereas in women it has dropped (the main reduction occurring during the 1970s).¹⁶ In 2 American studies performed in the south of Michigan¹⁷ and around Rochester (Minnesota),¹⁸ the incidence of heart failure was found to have been stable since 1980 in both sexes. These results are surprising when it is remembered that the control of high blood pressure, one of the main causes of heart failure, has improved through the generalization of treatment. However, it can also be argued that this has prevented

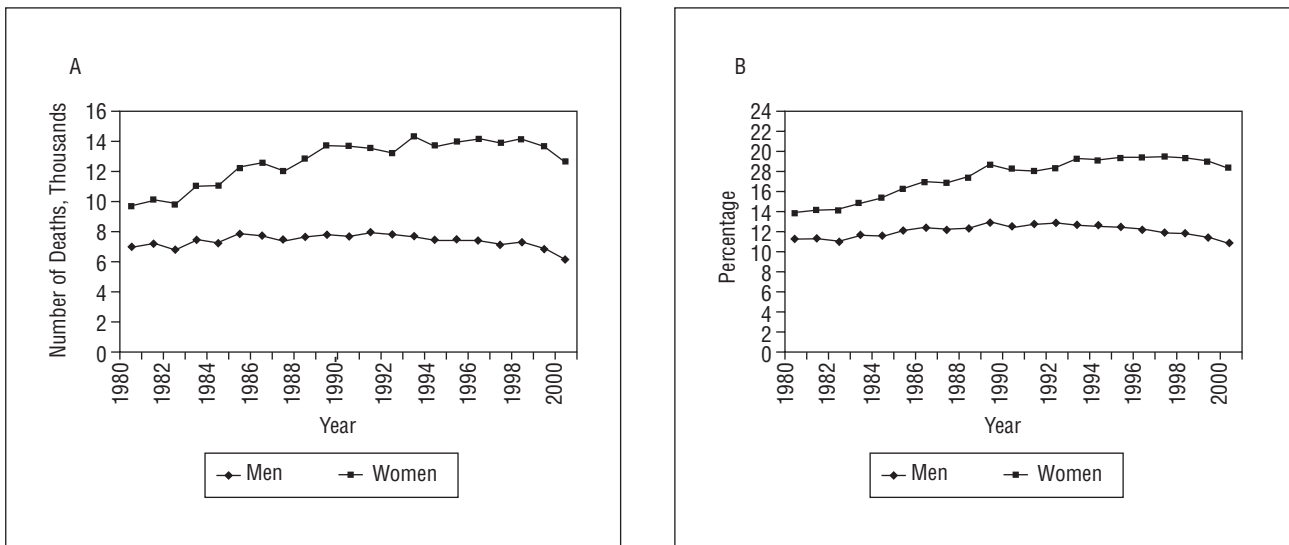


Fig. 2. A: number of deaths due to heart failure. B: deaths due to heart failure as a percentage of all cardiovascular deaths in Spain (1980-2000). Code 228 of ICD-9 for the period 1980-1998, and code I50 of ICD-10 for 1999-2000.

many coronary and cerebrovascular deaths and has increased the number of people who survive and remain at risk of developing heart failure. The reduction in the incidence of ischemic heart disease in some areas should also have reduced the incidence of heart failure. But again, this could be balanced out by the increased survival of ischemic heart disease patients who go on to develop heart failure. Finally, there is an epidemic of obesity and type 2 diabetes in the developed world, both of which are important risk factors for heart failure.

HEART FAILURE AND SURVIVAL

Heart failure is a progressive, lethal disease, even when adequately treated. Survival is determined by the follow-up of heart failure patients included in control groups in clinical trials, and by examining hospital records or the results of cohort studies involving the general population. Normally, the survival of patients included in clinical trials is better than that seen in population-based studies since the former tend to include younger patients with fewer accompanying ailments. The Framingham study also provides some of the best data on survival in heart failure patients. Five year survival (from time of diagnosis) is only around 50%^{19,20}—no better than for many forms of cancer—and is worse among older patients, those with more advanced disease, and those with serious concomitant disease.

Relatively few studies have been published on changes in survival among patients with heart failure in recent decades. Nonetheless, evidence from community-based¹⁶ studies and investigations performed at medical centers^{21,22} suggests that survival has improved

over the last 10 years. This improvement coincides with the increased use of therapies (such as the use ACE inhibitors and beta-blockers) that in clinical trials have been shown to reduce the mortality associated with heart failure. Paradoxically, this desirable improvement in survival also translates into greater numbers of people with heart failure, increasing the social burden.

This improvement in prognosis for people with heart failure is, however, smaller than that desired. The reasons for this are several. Firstly, heart failure is a syndrome with multiple causes. Many patients show preserved systolic function but have ventricular filling or valve problems, and neither ACE inhibitors nor beta-blockers appear to help them. Secondly, many patients with heart failure are women, are elderly, or have important comorbidity, and these groups have not normally been included in clinical trials. Finally, the clinical treatment of heart failure patients with low ejection fractions is sub-optimal, although recently it seems to have improved.²³⁻²⁸

MORTALITY ASSOCIATED WITH HEART FAILURE

The mortality associated with heart failure is calculated from death certificate data as incorporated into national vital statistics. Apart from hospital admissions, it is the only indicator that provides mortality data at the national level. Mortality figures provide information on the demographic impact of heart failure, although they usually underestimate its magnitude since the norms for coding cardiovascular death in national vital statistics prioritize ischemic heart disease

ahead of heart failure.

Heart failure is the third most common cause of cardiovascular death in Spain, after ischemic heart disease and cerebrovascular disease.²⁹ In 2000 it was responsible for 4% of all male deaths and 10% of all male cardiovascular deaths; among women these figures reached as high as 8% and 18% respectively. Heart failure mortality increases from northern Spain towards the south and the Mediterranean regions, and shows a similar pattern to the mortality associated with ischemic heart disease and cerebrovascular disease. It is also similar to that of angina prevalence.^{11,29} Heart failure mortality has descended progressively in both sexes since 1977, although it seems to have stabilized in persons of 85 years of age and over.²⁹ Despite this reduction, the total number of deaths caused by heart failure among women increased between 1980 and 2000 (Figure 2A), a result of the increased population size and its progressive ageing. Also among women, heart failure has become more important as a cause of death within the cardiovascular disease group (Figure 2B). As with the number of hospitalizations, the number of deaths due to heart failure is greater among women than among men.

The decreasing tendencies observed in Spain with respect to death due to heart failure are consistent with results from Canada, the USA,²⁹ and Argentina.³⁰ This is probably another manifestation of the reduced mortality associated with cardiovascular diseases as a whole, but is probably also due to giving priority to other causes of cardiovascular death ahead of heart failure on death certificates.

DIFFERENCES BETWEEN SYSTOLIC AND DIASTOLIC HEART FAILURE

Nearly all the above data correspond to "total" heart failure, i.e., they do not take into account whether the systolic function of the left ventricle is preserved (as shown by echocardiographic results). Though the ejection fraction cut-off point that defines systolic dysfunction has not been definitively established (it lies between 35% and 50% depending on the study), both clinical^{26,31} and population-based studies^{8,32} suggest that around 50% of heart failure patients have either normal or only slightly impaired systolic function. Because of selection criteria, clinical studies show heart failure with reduced systolic function to be more commonly recorded at cardiology departments than at internal medicine or geriatric departments.^{23,24}

The epidemiology and natural history of heart failure with diastolic dysfunction are poorly understood because of the difficulty in confirming this diagnosis with the procedures used in epidemiological studies. For this reason, these patients have not been included in the majority of clinical trials. The treatment criteria

for this problem are therefore based on less scientific evidence than those for heart failure with reduced ejection fraction. Until recently it was believed that diastolic heart failure had a better prognosis than systolic heart failure,^{24,32} especially in older patients,³³ but recent evidence suggests that their long term prognosis is similar.^{25,34,35} The recurrent hospitalization rates and healthcare costs for these conditions also appear to be similar.³⁶ Diastolic heart failure is more common in women and older people than systolic heart failure, and is usually preceded by many years of high blood pressure.^{34,35}

ASYMPTOMATIC SYSTOLIC DYSFUNCTION

Asymptomatic left ventricular systolic dysfunction (LVSD) is at least as common as heart failure: its prevalence is 3%-6%. However, several studies increase this range to 0.9%-12.9%, depending on their design, the characteristics of the study subjects, and the definitions used for LVSD and "asymptomatic."³⁶ The importance of LVSD is double: firstly it is an important risk factor for heart failure, and secondly it usually goes unnoticed and is frequently untreated, even though there is evidence that treatment reduces the incidence, number of hospitalizations and mortality due to heart failure.^{37,38}

DIFFERENCES BETWEEN THE SEXES

The prevalence, incidence and mortality of heart failure are actually somewhat higher among men than women. However, since these three indicators increase greatly with age, and since there are more elderly women than elderly men, the total number of cases and deaths caused by heart failure is greater among women.

After adjustment for age, the survival of women with heart failure is greater than that of men.²⁰ The reasons for this, are not clear. However, heart failure with conserved systolic function is more frequent in women, and therefore many studies may have recorded a higher number of false positives among them, i.e., the clinical symptoms leading to a diagnosis of heart failure may have had other causes.³ Moreover, differences in survival between the sexes tend to attenuate when adjustments are made for the ejection fraction and blood pressure.³⁹

Compared to men, women with heart failure usually show more symptoms for similar ejection fractions,⁴⁰ are older, more commonly suffer diabetes mellitus and high blood pressure, and less frequently suffer ischemic heart disease.^{24,31,34,35} Recent evidence shows that the response of women to some of the classic heart failure treatments can be different to that of men. For example, it would appear that digoxin treatment increases mortality among women with

heart failure and LVSD—something not seen among male patients.⁴¹ It should be remembered that women have been much less frequently included than men in clinical trials concerning heart failure treatments, but the above evidence does seem to suggest that the natural history of this disease is different in men and women.

DETERMINANTS OF HEART FAILURE

As mentioned earlier, the main precursors of heart failure are coronary heart disease and high blood pressure (which often appear together), followed by myocardial disease and valve dysfunction. Heart failure due to acute myocardial infarction is accompanied by systolic ventricular dysfunction more often than when due to high blood pressure. In the Anglo-Saxon world, coronary heart disease has increased in importance over recent decades as a cause of heart failure, while the importance of high blood pressure has shown a relative decline. The main risk factors for heart failure (diabetes, smoking, dyslipidemia, obesity and a sedentary lifestyle)^{15,42} are also those of its precursor conditions. Recent evidence suggests that higher homocysteine levels,⁴³ pulse pressure⁴⁴, and some plasma markers of inflammation (interleukin 6, C-reactive protein, tumor necrosis factor alpha)⁴⁵ are associated with an increased risk of heart failure, whereas moderate alcohol consumption is associated with a decreased risk.⁴⁶

COMMUNITY SCREENING FOR ASYMPTOMATIC VENTRICULAR DYSFUNCTION

The idea of opportunistic screening of the population for heart failure and ventricular dysfunction during medical contact with elderly patients has been suggested: the prevalence of heart failure is high among older people, there are effective treatments that can improve the quality of life and reduce the number of hospitalizations and mortality associated with the problem, and the earlier treatment begins the better the prognosis. Similar screening is performed for certain tumors. This type of screening would be more efficient (more cases of heart failure detected per 100 persons examined) if it were aimed at those patients at greatest risk, such as those with high blood pressure, diabetes, and those with a history of ischemic heart disease or other heart problems. Patients could also be selected according to the results of heart failure risk equations such as those used in the Framingham study. These estimate the risk of heart failure by considering age, left ventricular hypertrophy, heart rate, systolic blood pressure, whether the patient has diabetes mellitus, and evidence of previous myocardial infarction, valve disease or high blood pressure. More precise estima-

tions can be made if vital capacity and the possibility of cardiomegaly, judged from a recent chest X-ray,⁴⁷ are taken into account. People at greater risk are more likely to have left ventricular dysfunction; in these patients, the diagnostic efficiency of echocardiography is greater.

Community screening for LVSD is, however, a premature course of action.³⁶ Firstly, there is no optimum method for detecting LVSD. Echocardiography would be very expensive and impractical on a large scale, and the diagnostic validity of natriuretic peptides is less than perfect. Secondly, looking for LVSD would leave out a large number of people who might develop heart failure but maintain normal systolic function. Finally, the bulk of the evidence concerning the risk of developing heart failure with LVSD comes from clinical trials in which many of the patient types at greatest risk were not included.

THE HEART FAILURE EPIDEMIC

In the developed world, the increased prevalence of heart failure over recent decades and the number of hospitalizations associated with this syndrome, have led to its recognition as a 21st century cardiovascular epidemic. Demographic projections suggest that this problem will continue to increase among people over 65 years of age in the coming years. Given the frequency of heart failure in these older people, only a large reduction in the incidence of the disease, or a non-desirable reduction in survival, can stop the number of people suffering heart failure from increasing. The literature suggests that survival associated with the syndrome is improving, but that there is no appreciable reduction in its incidence. The control of risk factors such as high blood pressure and ischemic heart disease (the main causes of heart failure in Spain) is the only way to attenuate the foreseeable increase in the frequency of this disease in the near future.⁴⁸

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