

Prevalence of Heart Failure in the Spanish General Population Aged Over 45 Years. The PRICE Study

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Introduction and objectives. Congestive heart failure is associated with substantial morbidity and mortality and both its incidence and prevalence are high. Nevertheless, comprehensive data on this condition in Spain are lacking. The aim of this study was to determine the prevalence of congestive heart failure in Spain.

Methods. A demographic study which involved the participation of 15 healthcare centers throughout Spain was carried out. In each health area, a random sample was taken of the population aged 45 years or more. These individuals were examined by their primary care physicians, who made their diagnoses using Framingham criteria. Individuals who satisfied criteria for congestive heart failure were referred to a cardiologist for confirmation of the diagnosis and for echocardiography.

Results. Overall, 1776 individuals were evaluated. Their mean age was 64±12 years (range, 45-100 years) and 44% were male. Of these, 242 were referred to a cardiologist. The weighted prevalence of congestive heart failure was 6.8% (95% confidence interval [CI] 4-8.7). The prevalence was similar in men (6.5%, 95% CI 4.7-8.4) and women (7%, 95% CI 4.4-9.6). When analyzed by age, the prevalence was 1.3% (0.4%-2.1%) in those aged 45-54 years, 5.5% (2.4%-8.5%) in those aged 55-64 years, 8% (4.2%-11.8%) in those aged 65-74 years, and 16.1% (11%-21.1%) in those aged over 74 years.

Conclusions. Prevalence of congestive heart failure in Spain is high, at about 7%-8%. The prevalence was similar in males and females, and appeared to increase

with age.

Key words: Heart failure. Prevalence. Epidemiology.

Prevalencia de la insuficiencia cardiaca en la población general española mayor de 45 años. Estudio PRICE

Introducción y objetivos. La insuficiencia cardiaca congestiva (ICC) tiene elevadas incidencia, morbilidad y mortalidad y una gran prevalencia. Sin embargo, no hay datos directos sobre este aspecto en nuestro país. El objetivo de nuestro estudio es evaluar la prevalencia de ICC en España.

Métodos. Se diseñó un estudio poblacional en el que participaron 15 centros repartidos por toda España. Se seleccionó de forma aleatoria una muestra de la población de 45 o más años de edad atendida en cada área de salud, que fue estudiada por sus médicos de atención primaria. Se utilizaron los criterios de Framingham para el diagnóstico. Las personas con criterios de ICC fueron remitidas a una consulta de cardiología para confirmación diagnóstica y realización de ecocardiograma.

Resultados. Se evaluó a 1.776 personas, con una media ± desviación estándar (intervalo) de edad de 64 ± 12 (45-100) años; eran varones el 44%. Se remitió a cardiología a 242 pacientes. La prevalencia ponderada de ICC fue del 6,8% (intervalo de confianza [IC] del 95%, 4%-8,7). La prevalencia fue similar en varones (6,5%; IC del 95%, 4,7-8,4) y en mujeres (7%; IC del 95%, 4,4-9,6). Por edades, la prevalencia fue del 1,3% (0,4%-2,1%) entre los 45 y 54 años; el 5,5% (2,4%-8,5%) entre 55 y 64 años; el 8% (4,2%-11,8%) entre 65 y 74 años, y el 16,1% (11%-21,1%) en personas de 75 o más años.

Conclusiones. La prevalencia de ICC en España es alta, en torno a un 7-8%. La prevalencia es similar en varones y mujeres, y parece aumentar con la edad.

Palabras clave: Insuficiencia cardiaca. Prevalencia. Epidemiología.

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Centers and investigators who participated in the PRICE study are shown in the Appendix.

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ABBREVIATIONS

CHF: congestive heart failure

PRICE: estudio de prevalencia de insuficiencia cardiaca en España (prevalence of heart failure in Spain study)

INTRODUCTION

Congestive heart failure (CHF) is becoming one of the main public health problems in developed countries. It is the cause of significant morbi-mortality in the general population and its incidence and prevalence are increasing due to the ageing of the population, improvements in health care, and improved survival in those with chronic diseases. The situation is exacerbated by the fact that CHF is the final stage of many heart diseases which have also seen significant improvements in survival.^{1,2} Although treatment and disease course for many heart conditions have improved, morbi-mortality in CHF has not decreased significantly. This is likely due to the fact that the CHF population are older and have higher rates of comorbidity.^{3,4} The increase in morbidity is reflected in increased hospital admissions, with CHF being the main cause of medical hospital admissions in patients over 65 years of age.^{4,5} On the other hand, age-adjusted mortality rates have decreased slightly in Spain.^{4,5}

Although in many developed countries CHF appears to have become more prevalent in recent years,^{5,6} studies of prevalence are usually not carried out at the national level. In Spain, the only population-level study to date was performed in Asturias over 10 years ago (in 1996). The results indicated a prevalence of 5% in the population aged 40 years or over.⁷ The prevalence of CHF in Spain is likely to have increased since then, due to the factors mentioned above. The present paper presents the results of the PRICE (Prevalencia de Insuficiencia Cardiaca en España, [Heart Failure Prevalence Study in Spain]) study. The study objective was to evaluate the prevalence of CHF in the general population aged 45 years or over in Spain.

METHODS

The PRICE study was sponsored by the Heart Failure, Heart Transplant, and Alternative Treatment Section of the Spanish Society of Cardiology, and made use of the CHF units that participated in the BADAPIC (Base de Datos en Pacientes con Insuficiencia Cardíaca [Patients

with Heart Failure Database]) registry.⁸ The 53 hospitals collaborating on the registry were initially sent an invitation to participate in the study.

The invitation included a brief survey to determine whether centers met certain requirements for inclusion in the study. These included having access and fluid communications with the corresponding primary care network as well as having capacity for the extra consultations and echocardiograms required by the study. Furthermore, all primary care centers in the corresponding health care area were required to provide a list of the entire population covered by the area, stratified by age and sex. Of the 53 centers contacted, 22 confirmed they would be able to comply with requirements. A total of 15 hospitals and the 55 health care centers corresponding to the same health care areas were included in the study (see Appendix): 3 in Asturias; 2 in Andalucía, Aragón, País Vasco, and Galicia; and 1 in Castilla-La Mancha, Murcia, Valencia, and Cantabria. Fieldwork was carried out in 2004 and 2005.

Sampling Procedure

Each hospital was required to include a given number of individuals aged ≥ 45 . Individuals included were distributed between the participating centers in the health area and were selected by simple random sampling from the center's population register of individuals aged ≥ 45 years. A total of 2703 individuals were invited to participate through a letter from their primary care physician which described the study objectives and procedures.

Diagnostic Criteria and Clinical Examinations

All participants were examined by their primary care physician to determine whether CHF was present. The modified Framingham criteria were used to decide on the presence of CHF (Table 1). A diagnosis of heart failure was assigned when there was a previous diagnosis of CHF confirmed after hospitalization or when 2 major criteria or 1 major and 2 minor criteria were present on examination. The clinician visit included assessment of the prior history of heart failure and cardiovascular risk factors in the medical record, a physical examination, an electrocardiogram, and a chest x-ray. Participants with a diagnosis of heart failure or with uncertain diagnosis were referred to the hospital for examination by a cardiologist. The cardiologist repeated the physical examination and evaluated the results of the ECG and chest x-ray. A Doppler echocardiogram was also performed. A final diagnosis of CHF was established when there were positive Framingham criteria and significant organic or functional anomalies on the Doppler echocardiogram (ejection fraction $< 45\%$; diastolic dysfunction with abnormal relaxation pattern, distensibility or pseudonormal pattern; a minimum of

TABLE 1. Framingham Criteria (Modified) for the Diagnosis of Left Heart Failure

Major criteria	Paroxysmal nocturnal dyspnea Rales S3 gallop Radiographic cardiomegaly Radiological signs of pulmonary edema
Minor criteria	Dyspnea on ordinary exertion Nocturnal cough Tachycardia >120 beats/min Radiological pleural effusion Weight loss >4.5 kg in 5 days in response to diuretic treatment

moderate mitral or aortic valve damage, or left ventricular hypertrophy). The cardiologist also established CHF etiology, functional capacity, and type of CHF (depressed systolic function was defined as left ventricular ejection fraction <45%, and preserved systolic function as ejection fraction ≥45%). In order to analyze the reliability of the primary care diagnosis and the agreement between specialists and primary care physicians, a random sub-sample of 5% of participants without clinical indications of CHF was included at the primary care visit and referred for assessment by a cardiologist. The hospital evaluation included a Doppler echocardiogram.

Statistical Analysis

To take into account limitations in sample selection, the sample was weighted to ensure that it was representative of the Spanish general population by age and sex. Weights were defined as the inverse of the probability of selection, assuming that the 15 hospitals selected were a random sample of all hospitals in Spain. It was also assumed that, while the prevalence of CHF may differ between different regions of Spain, these differences would not be related to the fact that a given

hospital was part of the heart failure unit network. Likewise, we assumed that prevalence would be unrelated to the hospital’s degree of access to primary care in the area. Finally, the weights assigned were readjusted so that the weighted sample had the same distribution by age group and sex as the population of Spain according to the 2001 census data. The weight assigned to each patient reflects the number of individuals in the Spanish population represented by that patient, taking into account age group and sex.⁹ The sum of all the weights is therefore equal to the size of the Spanish population aged 45 or over. Weighted prevalences for CHF were calculated for the population as a whole as well as for specific age groups and by gender.

Cohen’s kappa statistic¹⁰ was used to estimate agreement between the primary care physician’s and the cardiologist’s assessment. Results are presented as the percent agreement. The cardiologist’s diagnosis (which included the results of the Doppler echocardiogram) was considered the gold standard.¹¹

Point estimates and 95% confidence intervals (CI) are used to present the results. The stepwise sampling strategy was taken into account when calculating the degree of precision (the confidence intervals of the estimates).

RESULTS

A total of 1776 individuals participated in the study (66% of those invited to participate). Of these, 242 were evaluated both at primary care level and by a cardiologist. The distribution of the final sample of participants evaluated only in primary care and at both primary care and hospital level is shown in Table 2. Table 3 shows the characteristics of the study sample. The mean (standard deviation [SD]) of the population evaluated was 64 (12) years; 44.1% were male. Table 2 also shows the sample distribution by 10 year age splits and sex. Almost 64% of participants were living in towns or cities at the time of the study, compared to 36% who were living in rural locations. A total of 6.7% of the sample had a prior history

TABLE 2. Distribution of Participants Attended in Primary Care and in Both Settings Means (Primary Care and Hospital) by Age Group and Sex

	Setting for Evaluation	Men, No. (%)	Women, No. (%)	Total, No. (%)
Age, y				
45-54	Primary care	212 (27.1)	255 (25.7)	467 (26.3)
	Both	14 (14.3)	31 (21.5)	45 (18.6)
55-64	Primary care	217 (27.7)	268 (26.9)	485 (27.3)
	Both	32 (32.7)	29 (20.1)	61 (25.2)
65-74	Primary care	187 (23.9)	252 (25.4)	439 (24.7)
	Both	25 (25.5)	45 (31.3)	70 (28.9)
>75	Primary care	167 (21.3)	218 (22)	385 (21.7)
	Both	27 (27.6)	39 (27.1)	66 (27.3)
Total	Primary care	783 (44.1)	993 (55.9)	1776
	Both	98 (40.5)	144 (59.5)	242

TABLE 3. Sample Characteristics (n=1776)

	%
Resident in urban area	63.9
Educational level	
Primary	73.5
Middle	22.5
High	4.1
Personal antecedents	
Ischemic heart disease	6.7
Diabetes	14.1
Hyperlipidemia	33.8
High blood pressure	30.9
Obesity	29.5
Cigarette consumption	
Active smoker	14.9
Ex-smoker	19.6
Previous diagnosis of heart failure	4.1

of ischemic heart disease; 14.1% of diabetes; 29.5% of high blood pressure; 30.9% of hyperlipidemia; and 14.9% were current smokers. Of the overall sample, 4.1% had been diagnosed with heart failure during a previous hospital admission.

The prevalence of CHF, by age group and sex, are shown in Table 4. In the overall sample, 6.8% (95% CI, 4.9-8.7) met the study definition for CHF. No difference in prevalence rates was observed by sex (6.5% in men compared to 7% in women), but there were differences by age group, with prevalence rising rapidly with age. In the 45 to 54 year-old age group, prevalence was 1.3%, compared to 5.5% in the 55-64 year-old age group, 8% in the 65-74 year-old age group, and 16.1% in those aged 75 or over (Table 4). The increase with age was similar in men and women (Table 4). Of those with CHF, 52% had depressed systolic function (left ventricular fraction <45%) and 48% had preserved systolic function (ejection fraction ≥45%).

There was 86% agreement between primary care physicians and cardiologists in terms of diagnosis. Agreement on specific criteria was ≥90%, except for cardiomegaly (85.6%) and dyspnea on exertion (87.2%).

DISCUSSION

According to the results of our study, the prevalence of heart failure in Spain is high, at around 6.8% of the population aged 45 or over. The prevalence rate is similar in men and women and clearly increases with age, to 16% in men and women aged over 75 years. Prevalence is 8% in the 65-74 age group, 5.5% in the 55-64 age group, and 1.3% in the 45-54 age group. The overall prevalence found here (6.8%) is slightly higher than that found by Cortina et al⁷ in Asturias 8 years earlier

TABLE 4. Weighted Prevalence by Age Group and Sex

	Men	Women	Total
Age, y			
45-54	1.3 (...-2.7)	1.2 (...-2.6)	1.3 (0.4-2.1)
55-64	7.4 (1.3-13.5)	3.6 (1-6.2)	5.5 (2.4-8.5)
65-74	7 (2.5-11.6)	8.8 (4.1-13.4)	8 (4.2-11.8)
>75	15.6 (9.4-21.8)	16.4 (9.7-23)	16.1 (11-21.1)
Overall	6.5 (4.7-8.4)	7 (4.4-9.6)	6.8 (4.9-8.7)

Data are shown in percentages (95% confidence interval).

(5%). In the earlier study, a total of 391 individuals were evaluated and the clinical examination was performed by cardiologists; in over 80% of cases, the examination included evaluation using Doppler echocardiogram. Our study, on the other hand, was based on assessment in primary care, which could lead to an underestimate of heart failure prevalence. Nevertheless, there was substantial agreement (86%) between assessments made in primary care and those made by the cardiologist.

The prevalence rate for heart failure observed here represents a considerable increase from figures published over the last 10 years for western countries.^{5,6} Data from the Framingham study showed a prevalence for CHF of 1% in individuals over 40 years of age.¹² Cleland et al¹³ also reported a prevalence of 1%, with an additional 2% of patients showing signs and symptoms of CHF after an exhaustive exploration (giving a total of 3%). In Minnesota, in the county of Olmsted, a prevalence of CHF of only 2.2% was recorded between 1997 and 2000.¹⁴ The prevalence of CHF doubles with every decade of age,^{7,13} a finding which was confirmed in our study and which might, to a large extent, explain the increase in prevalence in CHF over the last 10-20 years. Another contributing and related factor, is the improvement in treatments for CHF and the associated decrease in mortality, as indicated in recent studies from Europe³ and the United States.¹⁵ In Spain, mortality from CHF has also decreased recently,^{4,5} although it remains the third most important cardiovascular cause of death after ischemic heart disease and stroke, in men and women. It has been shown to be responsible for 15% of total cardiovascular mortality (11% in men and 19% in women).¹⁶

Data from some studies have confirmed the increase in the prevalence of CHF in recent years^{16,17} and suggest that prevalence will rise even more over the next 10-15 years. Stewart et al¹⁷ calculated that the prevalence of CHF in Scotland will increase by 31% in men and 17% in women between the year 2000 and 2020. Our results are in line with those forecasts, as well as with previous observations of a high prevalence of heart failure in

women¹⁶ and in older age groups.¹⁷ As the average age of the population will almost certainly continue to rise and as life expectancy in women continues to exceed that of men, a heart failure “epidemic” appears increasingly likely, with the consequent need for greater treatment resources. Another interesting aspect of our data is that, of the total of heart failure cases found, ejection fraction was preserved in approximately half. This supports the results of recent studies in the United States.¹⁴

Limitations

Our study has some limitations which stem largely from the methodology used. The logistic complexity of a study of this type, which was performed throughout Spain, largely in primary care centers, and without financial remuneration for participating investigators, meant that the initial selection of centers was not randomized as it was considered essential to include investigators who would be committed to the study. This meant that large urban areas are under-represented and could, in addition, theoretically lead to a bias towards a higher number of CHF diagnoses. Nevertheless, confirmation of the diagnosis by cardiologists reduces that possibility. Agreement between primary care physicians and specialists, both in terms of the overall diagnosis of CHF as well as on specific clinical criteria, was very high (86% for the overall diagnosis). Another important source of bias could have been in the final selection of patients, though this was reduced by using random selection, and an acceptable degree of participation was also achieved. Finally, we have no information regarding prevalence in institutionalized patients and, in spite of the precautions taken and the high level of agreement between primary and specialist care, the possibility of under-diagnosis in primary care remains. Both aspects might lead to an underestimation of true prevalence rates.

CONCLUSIONS

Taking into account the limitations mentioned above, the results of our study indicate that the prevalence of CHF in Spain in the population aged 45 years or over is high, at almost 7%. The prevalence rates are similar in men and women, and increase with age. These data, which are the first to be obtained in a nationwide study, can be used for future estimates of the magnitude of CHF in Spain and, with the aid of real local data, can be used

to guide resource allocation for the management of the disease.

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Vistalegre Health Care Center Santomera Health Care Center	
13. Hospital de Basurto (Bilbao) Lead investigator	Nekane Murga Eizagaecheverria Begoña Goiria Bikondi Purificación de Cos Rodríguez
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APPENDIX. PRICE Study Investigators *(Continued)*

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