

## The «Epidemic» of Heart Failure

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It is generally agreed that heart failure (HF) is a major public health problem in the Western world. Its increasing incidence, which is related to the aging of the population and, perhaps, to improved survival after acute coronary syndromes, is the reason why it can be described it as a true epidemic.

Nevertheless, it is possible that the published figures on HF have been distorted due to series of causes, including the lack of precise and unified diagnostic criteria, the scarcity of trustworthy sources of data, the use of a variety of measurement tools, and the absence of large prospective registries. In addition, important differences exist in the data on HF from different geographic areas, which is why the extrapolation to other societies or countries of data collected in a given population can lead to major errors.

The fact that epidemiological studies of HF found in the medical literature often report discordant results only confirms this.

In this issue of the journal, Boix et al<sup>2</sup> publish an interesting article on mortality attributed to acute coronary syndrome in Spain. This retrospective study analyzes data collected from death certificates and the NMDS (National Minimum Data Set), a standardized system for coding hospital releases. The authors conclude that deaths due to HF are responsible for 4.8% of total mortality in Spain, and indicate differences by sex and geographic area.

To better assess the ramifications of this publication, we must first know the findings on HF that have been reported by the main publications in this field, and understand the difficulties and limitations of epidemiological studies of HF.

### FIGURES ON THE WORLD-WIDE «EPIDEMIC» OF HEART FAILURE

In the U.S., where health information systems are more developed (probably due to a close relation with the financing of the system), a prevalence of 5 million patients with a diagnosis of HF has been recorded, with an incidence of 500 000 new cases every year. These patients require 12 to 15 million office visits and 6.5 million hospitalization days every year. From an economic point of view, this is an expense of 38 000 million dollars, equivalent to 5.4% of the annual U.S. health budget. The volume of sales of specific medications for this process was 500 million dollars in 1999. The number of hospitalizations in which HF was the main diagnosis doubled in the last 10 years, and 300 000 Americans die every year as a result of this syndrome as a primordial or closely related cause.

In Europe, several partial epidemiological studies have been made, which are generally retrospective and have different inclusion criteria. In most of these studies, the diagnosis of HF is made by clinical and radiological criteria, like those used in the Framingham study. On other occasions, either the Boston criteria, a more refined index, have been used, or methods that include echocardiographic criteria like those proposed by the Task Force on Heart Failure of the European Society of Cardiology, which have recently been applied to small cohorts. This variability makes it difficult to process prevalence and mortality data, especially when a large part of the information comes from primary care physicians or different specialties, which tends to be less rigorous overall (or so it is thought) than that contributed by cardiologists, who use more precise diagnostic procedures, like echocardiography.

Generally speaking, it is estimated that Europe has an annual incidence of 1.3 cases per 1000 inhabitants among persons over 25 years of age. The incidence increases progressively by age group, reaching 11.6 per 1000 in persons over 85 years.

There is little data, and it is probably not very rigorous, regarding mortality due to HF. This is probably due to the immaturity of the information systems and to the lack of a precise definition that

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would allow consistent coding of the processes and, more importantly, the causes of death. In this context, the contribution of Boix et al is, at the very least, a relevant approach to the reality of the problem in Spain.

### **LIMITATIONS AND DIFFICULTIES OF EPIDEMIOLOGICAL STUDIES OF HEART FAILURE**

The major trials of drugs in HF have «deformed» the image of the average patient with this syndrome. In these trials, patients are mainly middle-aged men with severe left ventricular systolic dysfunction and a high percentage have heart disease due to coronary artery disease. In contrast, the main epidemiological studies of HF have revealed a very different scenario, with a population with a large proportion of women, a much older mean age, a high percentage of patients with diastolic HF, and a greater proportion in which the condition is probably due to arterial hypertension.

Is it possible, however, to know the epidemiology of HF with any certainty? In all sincerity, at present the answer has to be no.

A key part of any epidemiological study is defining the event to be studied. In spite of the extended and apparently precise use of the terms «heart failure» and «cardiac insufficiency», their practical application involves more difficulties than those evident at first sight. The symptoms of this complex syndrome are not very specific and often do not allow an adequate diagnosis without other more objective tests. HF is basically a disease of older people, who frequently present comorbidity (respiratory, renal, and hepatic failure, etc.) that makes the differential diagnosis difficult.

When referring to HF in the real world, many authors note that it is basically a clinical syndrome characterized by two cardinal symptoms, dyspnea and fluid and salt retention. Both data are sensitive, but not very specific, which is why their evaluation is subject to interobserver variability. As commented previously, the diagnosis of HF is made by professionals with different qualifications, so diagnostic precision varies widely.

For this reason, other authors estimate that hospitalization may be the most precise indicator of the real status of congestive HF. A factor weighing against this are new tendencies in HF management based on the use of outpatient visits, day hospitals, at-home visits, etc. Such innovations could change the perception of the problem in different countries, regions or communities, depending on the degree to which they are implanted in the healthcare system. Another complication is the significant number of patients with forms of HF that are not very symptomatic, which would be overlooked by

epidemiological studies. In a study by McDonagh et al, approximately half of the patients with ejection fraction less than 30% in a population between 25 and 75 years of age did not have evident symptoms of HF.

As far as the prognosis of HF in real life goes, the results of epidemiological studies again correct the figures reported in clinical trials, revealing a higher than expected mortality (although a slight improvement in the prognosis of HF with the passage of years is observed, which is attributable to better treatment of the syndrome).

Coronary artery disease is the fundamental cause of HF, together with hypertension, and is present in almost 60% of cases. The prognosis and evolution of HF of ischemic origin is worse than in HF due to other causes. The improvement in survival after acute coronary syndromes with modern treatment has been postulated as one of the reasons for the increased incidence of HF. Nevertheless, this was recently questioned by Guidry et al, in an analysis of the population of Framingham in the periods 1950-1969 and 1980-1989, which showed no substantial differences between periods.

The pathophysiology of HF has prognostic implications. It is estimated that almost half of the patients have diastolic HF with conserved contractile function, which indicates a more favorable prognosis, and probably should be set apart in epidemiological studies of prognosis and mortality.

### **EPIDEMIOLOGICAL STUDIES ON HEART FAILURE IN SPAIN. THE ARTICLE OF BOIX ET AL**

In 1992, the National Minimum Data Set (NMDS) was introduced for the purpose of coding hospital discharge diagnoses according to the International Classification of Diseases, versions ICD-8 and ICD-9. In a few years it has become a basic instrument for information on hospital morbidity and mortality in Spain. Important gaps exist in coding criteria, especially with regard to causes of death, which are similar to those of the discharge diagnoses noted by physicians in clinical reports. All this, in spite of the achievements attained, affects the retrieval and usability of results.

Some authors maintain that the introduction of these coding systems may distort perceptions of the clinical problems. Stewart, of the Department of Public Health of the University of Glasgow, has indicated that the increased number of cases of HF recorded in recent years could be distorted by factors like administrative pressures to incorporate a second or third diagnosis (the diagnosis of «heart failure» often appears as an associated diagnosis instead of the main diagnosis). Another factor could be increased sensitivity to the need to identify HF in initial stages in patients with

cardiac structural disturbances, using precise diagnosis procedures like echocardiography or radionuclide scans. In this sense, the Scottish hospitalization registry indicates that 43% of admissions for HF had coronary artery disease as the first diagnosis, and 18% of them corresponded to acute myocardial infarctions in which signs of ventricular failure were evident.

On the other hand, there may be important methodological variations in data retrieval from the NMDS. For example, in their study Boix et al used the diagnostic codes 427.0 (congestive heart failure); 427.1 (left ventricular insufficiency); 420.0 (myocardial heart failure); 428.1 (left heart failure), and 428.9 (unspecified heart failure). However, codes like 402 (heart failure due to hypertension), 425.4 (primary cardiomyopathy), 425.5 (alcoholic cardiomyopathy), and 425.9 (secondary cardiomyopathy) are excluded. This does not reduce the validity of their study, but underlines the variability of criteria that can be used in different epidemiological studies.

Although the data of the NMDS for hospitalizations are reaching an important level of precision and quality in Spain, the same cannot be said of the data collected through medical death certificates which, among other things, are not subject to any type of audit.

In Spain, since 1974 (OM-764/74) when the Health and Mortuary Police Regulation was published, doctors who certify a death are required to define the causes of death according to a Classification of Cadavers. This classification distributes the causes of death between immediate, intermediate and fundamental causes, although precise definitions of these categories do not exist. The data collected are compiled in the *Statistical Death Bulletin* of the National Institute of Statistics. Although some rules for completion are given in the form, there are no clear criteria, so, in my opinion, the information that we can obtain for a specific process is not very trustworthy. In addition, there are no possible auditing mechanisms.

Boix et al report a surprising rise in the mortality due to HF in men of between 25 and 34 years of age in the 1980s and 1990s, which they attribute to the possible impact of acquired immunodeficiency syndrome (AIDS) and drug addiction, especially to cocaine. AIDS only produces HF in terminal stages and in a relatively exceptional way. Other manifestations like pericarditis or asymptomatic myocarditis are more frequent. Doubts exist as to whether the etiopathogenic mechanism would be direct involvement of the cardiomyocytes by HIV, the action of opportunistic pathogens like *Toxoplasma gondii*, or the development of lymphomas that affect the heart. In any case, the incidence of these complications is very low, which in no way explains this increment in the incidence of mortality due to HF.

Something similar could be said of cocaine addiction. This drug, whose consumption in Spain has increased exponentially since the 1990s, can induce adrenergic overstimulation by inhibiting the presynaptic reuse of noradrenaline. This mechanism can induce arrhythmias, sudden death, or acute myocardial infarction. Cardiomyopathy only occurs exceptionally, and in many cases is even reversible.

## EPILOGUE

With the clinical criteria used in most of the epidemiological studies currently available, it is difficult to know the true situation of the incidence and mortality of HF. The clinical trials, which invariably exclude women and patients over 75 years old, do not help much to understand the reality of this process. The fundamental tool of epidemiologists in the 21st century will be prospective registries using more precise definitions of HF to collect data using modern systems of health information.

The use of Doppler echography and certain biochemical or molecular determinations like cerebral natriuretic peptide («molecular epidemiology») will lead in the next few years to a much more precise knowledge of the magnitude of the problem. At the moment, with regard to epidemiological studies of HF «the jury is still out.»

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