

Is Preventing Heart Failure a Real Option?

¿Prevenir la insuficiencia cardíaca es una opción real?

*Making predictions is very difficult,
especially about the future*

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INTRODUCTION

Heart failure (HF) is becoming an epidemic of great proportions and therefore, as in vascular disease, it may be time to think about whether its development can be prevented.

However, there is no updated data on the key components of this epidemic, so we should review the latest large population registries that are representative of a community or a nation and evaluate the incidence of new HF occurrence and its prevalence in the population at a specific time.

Somehow, incidence is an abstract concept, since it refers to the development of HF with a standard rate. This estimation is done so that the incidence of the disease is independent of the changes in the population. It corrects for a similar age at an initial time, even from other regions, so that it can be compared with other populations, either its own or from other countries with a similar age. Conversely, prevalence refers to the real HF rate at a given time.

It is necessary to compare the current epidemiology of congestive heart failure (CHF) with the preceding Framingham populations with which the risk scores of HF were developed to predict the occurrence of HF in the next 4 years, (1) because there may be changes in demography, changes in prevalence and, obviously, in treatment and control of possible risk factors (for example hypertension and ischemic heart disease). But there could also be other important reasons, such as changes in diagnostic criteria. Even more, since HF is really a syndrome and not a disease, diagnosis is a challenge for its interpretation and may vary over time, as well as survival, which may also change among the prevalent cases of each period.

EPIDEMIOLOGY IN SWEDEN BASED ON 2.1 MILLION INHABITANTS BETWEEN 2006 AND 2010

We used the data from the greater Stockholm region, Sweden, which comprised 2.1 million inhabitants in 2010, (2) and included all the consultations in primary and secondary care (defined as specialist outpatient care), and all hospitalizations,

This cross-sectional investigation involved the entire population of patients in the Stockholm region who were registered with a primary or secondary diagnosis of CHF (CHF-10 code 150) in at least one

primary care consultation (from 2003 to 2010), secondary care (from 1997 to 2010), or during hospitalization (from 1997 to 2010). Comorbid conditions were identified in patients in 2010 looking for the diagnoses recorded for chronic diseases.

In 2010, a total of 88,038 patients (51% women) were found with diagnosis of CHF: The crude prevalence of HF was 1.8%, similar for men and women. But the estimated prevalence for all Sweden was 2.2%. The average age in 2010 was 77 years, with more than 90% of patients 60 years of age or older. The prevalence among men exceeded that of women for all age groups.

The prevalence of HF between 2006 and 2010 showed a weak trend towards temporary decline in women ($p=0.044$) but no changes in men ($p=0.25$).

The crude incidence in 2010 was 310/100,000 person-years, similar in men and women. (Figure 1) The estimated incidence for all of Sweden was lower in women (370/100,000 person-years) than in men (390/100,000 person-years; $p < 0.001$). The average age for the first recorded diagnosis of HF for incident patients in 2010 was 77 years (women 80 years, men 74 years; $p < 0.001$). There was a temporary decreasing trend of 0.9/1,000 person-years in absolute terms (e.g. 24% relative decrease, $p < 0.001$) between 2006 and 2010. (Figure 1) This tendency was not different between men and women.

The estimated mortality across Sweden, after adjusting for demographic composition, was 3.1/1,000 person-years higher in women than in men. Average age of death for patients with HF in 2010 was 87 years in women and 83 years in men, $p < 0.001$. Mortality decreased by 0.5/1,000 person-years in absolute terms (e.g. 19% relative decrease; $p < 0.001$) between 2006 and 2010, both in women and men.

When age was taken into account, the risk of all-cause mortality was higher in men than in women (1.29, 1.24-1.34, $p < 0.001$). This higher risk also remained unchanged after adjusting for comorbidities. Hypertension was the most common cardiovascular comorbidity, followed by ischemic heart disease, atrial flutter/fibrillation, diabetes, stroke and COPD. Five-year survival, adjusted for age, was associated to pre-existing comorbidities.

THE CONTEMPORARY EVALUATION OF HEART FAILURE IN OLMSTED COUNTY (MINNESOTA) FROM 2000 TO 2010

A study was conducted in Olmsted County (Minnesota), with an approximate population of 144,248 persons according to the 2010 census, mostly middle class

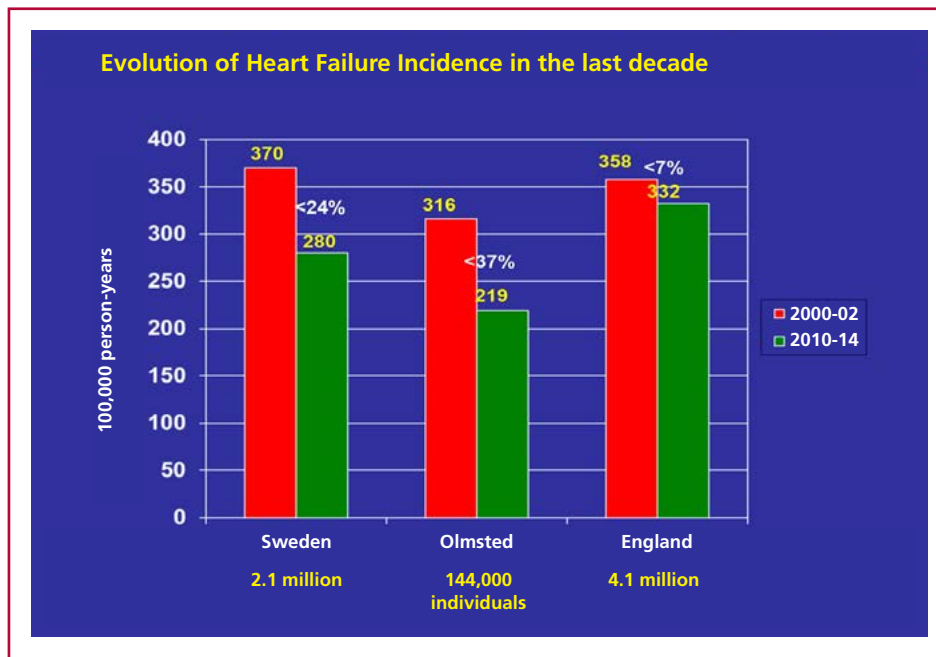


Fig. 1. Heart failure incidence

and with a lower rate of poverty (8.0% vs. 15.4%) than the total population of USA in 2010. (3)

The peculiarity is that medical care is practically self-contained within the community, and the largest health care provider is the Mayo Clinic. The medical records of all sources of care are indexed and linked via the Rochester Epidemiology Project.

The percentage of patients who did not grant authorization to investigate was globally low (4.2%) and stable during the study period.

The diagnosis of HF was identified by the International Classification of Diseases, Ninth Revision (ICD-9, code 428) between 2000 and 2010.

The distinctive feature is that ejection fraction (EF) was consistently measured by echocardiography, all performed at the Mayo Clinic, so the EF measurement closest to the diagnosis of HF was recorded for each participant. A cutoff point of 50% was used to define HF with preserved EF (HFpEF) >50% or HF with reduced EF (HFrEF) <50%, according to the guidelines.

The population aged 20 years or more in Olmsted County, as determined by the census data of 2000 and 2010, was used as denominator for total HF, HFpEF and HFrEF rates. The rates were standardized directly according to the distribution by age and gender of the 2010 US population.

The proportion of cases with HFpEF was 52.5%; but over time it increased from 47.8% in the 2000-2003 period to 52.3% in the 2008-2010 period. In addition, in patients with HFrEF, the prevalence of diabetes and hyperlipidemia increased, as well as the burden of comorbid conditions.

The rate of HF incidence adjusted for age and gender declined substantially by 37.5% in the last decade, with an annual change of -4.6%. (Figure 1) This de-

cline applies to both men and women and for HFrEF and HFpEF in absolute and relative terms.

Mortality was frequently ascribed (54.3%) to non-cardiovascular causes; the first 3 categories of non-cardiovascular causes were respiratory, mental or behavioral health. In addition to age, the factors positively associated with all-cause mortality were diabetes, smoking and increasing number of comorbidities. Moreover, most hospitalizations (63%) were due to non-cardiovascular causes, probably reflecting the increasing burden of comorbidities in this population of elderly patients.

A substantial decline was found in both types of HF, although the decrease was greater for HFrEF. These findings in turn result in changes in the case mix.

TIME TRENDS IN THE INCIDENCE OF HEART FAILURE IN A POPULATION OF 4 MILLION INDIVIDUALS IN THE UNITED KINGDOM

The electronic clinical records of the Clinical Practice Research Datalink (CPRD) were used from 1985 to 2015, with anonymous data of approximately 4 million people, i.e. 7% of the population of the United Kingdom (UK), which is completely representative in terms of age, gender, and ethnic characteristics. The CPRD primary care records were linked with secondary hospitalization records of the Hospital Episodes Statistics Admitted Patient Care. (4)

Data were obtained for men and women 16 years of age and older, between 2002 and 2014, using the first HF record of the International Classification of Diseases, tenth revision (ICD-10) for both primary care and hospitalization.

To calculate the standardized rate, age and gender was applied to the population of the 2013 European

Population Standard.

Average age at the time of HF diagnosis was 76.7 years (49.0% were women), but from 2002 to 2014 it increased from 76.5 to 77.0 years, with adjusted difference of 0.79 years. Men smoked more than women and socioeconomically deprived individuals [according to the 2015 Index of Multiple Deprivation (IMD), a composite measure of relative deprivation at a small area level, with an average of 1,500 people] had a higher prevalence of smoking and were more likely to have body mass index (BMI) in the range of overweight and obesity than more affluent individuals.

In the standardized models by age and gender, the incidence of HF decreased significantly by 7% from 2002 to 2014 (Figure 1). However, there was an increase in the incidence in the very elderly (85 years or older) and in those younger than 55 years.

In contrast to the declining standardized incidence, the crude incidence increased by 2%, from 2002 to 2014, and the estimated annual number of new HF diagnoses increased by 12%, from 170,727 in 2002 to 190,798 cases in 2014, due to population growth, especially in the elderly groups.

The prevalence of HF, standardized by age and gender, increased slightly during the study period, from 1.5% in 2001 to 1.6% in 2014. Therefore, the absolute number of people living with HF in the UK increased by 23% in the study period, from 750,127 in 2001 (1.3% of the total population) to 920,616 in 2014 (1.4% of the total population).

Comorbidities were high (mean 4.5 simultaneous chronic diseases) and increased in time from 3.4 in 2002 to 5.4 in 2014. Overall, 79% of patients had 3 or more comorbidities, and they increased from 68% in 2002 to 87% in 2014.

The incidence of HF by age was 1.52 times higher in men than in women, particularly in younger people, around 45-54 years of age. Men were younger than women at the time of diagnosis.

At the same age and gender, patients in the most deprived quintile were more likely to experience 1.61 times greater incidence of HF than individuals with higher income. In addition, those with the greatest deprivation were 3.5 years younger at the time of diagnosis. Socio-economic inequalities were also visible in comorbidity rates.

Despite a modest decline in the standardized incidence of HF, there has been a 12% increase in the number of new cases. This is substantial, and by comparison it is similar to the total combined number of new cases of breast, prostate, lung, and colon cancer.

The prevalence of HF has increased even more substantially than the incidence, possibly as a result of longer survival after its diagnosis. Above all, despite a relatively stable standardized prevalence, we observe 23% increase in the absolute number of people living with HF.

The number of associated comorbidities was high and increased between 2002 and 2014 in parallel with the increase in age. The authors suggest that in addition to the increasing number of patients with HF,

their clinical management has become more complex and this is likely to be influenced by several factors, such as population aging, screening and diagnostic facilitation, medical understanding, and changes in risk factors. Non-cardiovascular comorbidities make a substantial contribution over time. (4)

The results of the study show that socioeconomically deprived status is not only associated with the standardized incidence of higher incidence of HF, but also a disease with an earlier onset and greater comorbidity rates.

The absolute number of cases and the increase in the prevalence of HF, with a tendency to older ages and a substantial increase in the number of associated comorbidities, indicate that management is becoming more complex and the prevention of the factors that develop HF could be a real option for its control.

HEART FAILURE IN LOW- AND MIDDLE-INCOME COUNTRIES AND THE FRAMINGHAM SCORE TO PREDICT THE OCCURRENCE OF NEW HEART FAILURE

There have been few registries in recent years in low- and middle-income countries, but the countries that have produced more registries have been India and China in Asia and Brazil and Argentina in America. (5)

The meta-regression of these studies' meta-analysis shows that in the last 20 years (from 1990 to 2010) hypertension has increased significantly, but ischemic heart disease has remained stable and unchanged.

However, the treatment that has proved to reduce hospitalizations and mortality is underutilized in these countries; only slightly more than 2 out of 3 individuals (68.9%) receive diuretics, a little more than half (56.5%) receive angiotensin-converting enzyme inhibitors (ACEI) and only one third receive beta blockers and mineralocorticoid antagonists (34.1 and 32.1%, respectively).

The latest registries support the use of different scores for men and women of the Framingham study to predict the development of new HF.

In the Swedish registry women were significantly different from men, because they were older (80 vs. 74 years), had more hypertension (73 vs. 69%), but lower ischemic heart disease (47 vs. 56%), fibrillation or atrial flutter (43 vs. 48%) and diabetes (24 vs. 30%).

In the Olmsted County (Minnesota) registry, women differed from men in that they were also older (78 vs. 72 years), significantly more hypertensive (89% vs. 74%), had more hyperlipidemia (78% vs. 68%) and diabetes (30% vs. 24%), but presence of ischemic heart disease was similar and low (32% vs. 29%).

Table 2 shows that the logistic regression coefficients to calculate the occurrence of HF in the next 4 years (period of new control in the Framingham study) was different in men and women. Electrocardiographic hypertrophy and a 20 mmHg increase in systolic blood pressure were more significant in women, as well as the presence of aortic systolic murmur and diabetes; but coronary heart disease demonstrated in the control electrocardiogram was higher in men. The

difference is that BMI appeared as a significant variable in women but not in men.

NOW WE RECOGNIZE VARIABLES OR RISK FACTORS FOR THE FUTURE DEVELOPMENT OF HF. WHAT OCCURRED WITH THEM IN THE LAST DECADES?

The Global Burden of Disease (GBD) (6) followed the evolution of these factors for 26 years (from 1990 to 2016). Surprisingly, during this period, systolic hypertension increased slightly but significantly, despite the different drugs available for its control and the concern of the population. This rise in hypertension could perhaps be due to the increase in that period of high BMI by 50%, sweetened beverage consumption by 47% and high fasting blood sugar by almost 30%. At the same time physical activity decreased slightly, despite the promotion of marathons in different countries. These findings were repeated specifically in Argentina.

The increase in population age and the persistence of these factors explain the continuous increase in the prevalence of HF, with the current characteristic of association with multiple comorbidities, which raise hospitalizations for non-cardiac causes.

WE ARE OVERWHELMED BY DISAPPOINTMENT BECAUSE PREVENTION OF HEART FAILURE DOES NOT SEEM FEASIBLE, BUT...

Unexpectedly, long-term studies with obesity surgery change our perspectives.

The ongoing Swedish Obese Subjects (SOS) study is a controlled intervention that compares the effects of bariatric surgery and conventional obesity treatment on morbidity and mortality. The purpose of a recent publication is related with the issue that concerns us, because it describes the effect of bariatric surgery on the incidence of new HF. (7)

Between 1987 and 2001, 4,047 patients, aged 37 to 60 years, with a BMI of 34/kg/m² or more in men and 38/kg/m² or more in women, were incorporated to the study and followed up for at least 20 years.

The surgical group included 2,010 individuals who expressed preference for bariatric surgery and the control group included 2,037 participants using an automatic balancing program of 18 variables.

Body weight dropped by 25% in the first year, with an average baseline BMI of 44/kg/m², 18% at 6 years and stabilized at 16% up to 20 years, with no changes in the control group.

Patients with bariatric surgery demonstrated a surprising reduction in HF of 35% (95% CI 46%-21%), and that occurred only after the first 6 years.

Also, hospitalizations for HF decreased by 37% (95% CI 51%-21%), as well as the need for treatment with beta blockers, ACEI and other receptor inhibitors and loop diuretics.

In the combined population, the onset conditions were independently associated with an increased risk of HF. They included advanced age, male gender, hypertension, diabetes, high levels of cholesterol and smoking, similar to the factors of the Framingham score cohort of the 70s, and the more recent records we have discussed.

It can also be seen that the risk of HF declines steadily in the quartiles with the greatest weight loss. Quartiles 1 and 2 with almost no weight loss are established as a reference point and quartile 3 with a decrease of -22 kg at 1 year significantly decreases HF by 25%. The fourth quartile that had the largest weight loss (mean -41 kg), presents the greatest risk reduction to almost half (49% 95% CI 70%-30%).

The important association between weight loss and prevention of HF seems to be real, since the cumulative incidence curve that reflects a beneficial effect of bariatric surgery does not occur until after 6 years, but continues to separate over time until 20 years. Therefore, the primary prevention of the SOS study requires a long-term follow-up for the effect of weight loss on the risk of HF to become apparent.

The prevention of HF is reinforced by the concomitant result of lower hospitalizations for HF despite lower use of drugs for its treatment. In addition, there is also a dose-response relationship between weight loss and HF prevention.

The question now is what happens to obese adolescents, who have persistence of obesity and comorbidities with decreased life expectancy, if they undergo bariatric surgery, compared with adults who were also obese in adolescence? (8)

In several hospitals in the United States, and with

Table 2. Patient characteristics according to the type of oral anticoagulant used.

Estimation of heart failure in the Framingham study								
Variable	Units	MEN			WOMEN			
		OR (95% CI)	p	Variable	Units	OR (95% CI)	p	
Age	10 years	1.51 (1.31-1.74)	<0.001	Age	10 years	1.65 (1.42-1.93)	<0.001	
LVH	Yes/No	2.47 (1.31-3.77)	<0.001	LVH	Yes/No	3.82 (2.50-5.83)	<0.001	
HR	10 beats/min	1.18 (1.08-1.29)	<0.001	HR	10 beats/min	1.11 (1.01-1.23)	0.03	
SBP	20 mmHg	1.17 (1.04-1.32)	0.007	SBP	20 mmHg	1.07 (0.96-1.20)	0.024	
CHD	Yes/No	4.99 (3.80-6.55)	<0.001	CHD	Yes/No	4.74 (3.49-6.42)	<0.001	
Valve disease	Yes/No	2.64 (1.89-3.69)	<0.001	Valve disease	Yes/No	4.03 (2.86-5.67)	<0.001	
Diabetes	Yes/No	1.25 (0.89-1.76)	0.2	Diabetes	Yes/No	4.00 (2.78-5.74)	<0.001	
				BMI	Yes/No	1.06 (1.03-1.09)	<0.001	

LVH: Left ventricular hypertrophy. HR: Heart rate. SBP: Systolic blood pressure. CHD: Coronary heart disease. BMI: Body mass index.

the contribution of Australia, the health effect of the Roux-en-Y gastric bypass was evaluated in a cohort of 161 obese adolescents (BMI >35 kg/m²) aged 13 to 19 years enrolled from 2006 to 2012 and a cohort of 396 adults (obese at 18 years) aged 25 to 50 years enrolled from 2006 to 2009. The two cohorts were participants in independent but related studies.

Although there was no significant difference in weight change at 5 years between adolescents and adults after surgery (-26% and -29%, respectively), it was significantly more likely that adolescents would have more complete remissions (normalization without treatment) of diabetes (86% vs. 53%) and hypertension (68% vs. 41%)

After adjustment for known confounders, the greatest remission in adolescents included a shorter duration of diabetes. Adolescents also achieved and maintained greater glycemic control without medication than adults, suggesting that they would have a greater opportunity to regain the secretory capacity of islet cells. This concept may lead to consider the possibility of surgery relatively quickly after the diagnosis of diabetes in adolescents with severe obesity. (8)

Also, the fact that they have greater remission of hypertension (over 51% more than adults) seems to provide additional evidence that adolescents have greater plasticity for the reduction of obesity complications than adults.

CONCLUSIONS

To the ironic and hopeless epigraph of the scientist Niels Bohr, that "making predictions is very difficult, especially about the future," we could answer with that of the hopeful artist Woody Allen who says, "I am interested in the future, as it is the place where I will spend the rest of my life" So despite the difficulties

of prediction, the future still interests us ... and very much. Therefore, before the question of the title, we could now establish that "preventing heart failure is a real option," without using the question marks.

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