

CARDIOVASCULAR DISEASE IN WOMEN. A STUDY INTO THE CURRENT SITUATION IN SPAIN

A Study of Cardiovascular Disease in Women in Spain: Conclusions and Final Recommendations

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This article details the conclusions and final recommendations of the study on cardiovascular disease in women in Spain carried out by the Spanish Society of Cardiology. Important differences were found between men and women in clinical characteristics, risk factors, diagnostic assessment, treatment and prognosis in most of the conditions studied, but particularly in acute coronary syndrome, heart failure and hypertension. In general, differences in diagnostic and therapeutic procedures work to women's disadvantage. The information available on atrial fibrillation and valvular heart disease is incomplete and studies focusing on these conditions are needed. There is also a need for a program of education and information to raise awareness of inequalities between the sexes both in the general public and among healthcare professionals, and for practical measures that will improve care for women with cardiovascular disease.

Key words: Cardiovascular disease. Prevention. Sex differences

A wealth of information exists from reliable sources, such as registries and studies carried out by the Spanish Society of Cardiology, its Scientific Sections and Affiliated Societies, on the care status, characteristics

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Proyecto de estudio sobre la situación de la enfermedad cardiovascular de la mujer en España: conclusiones y recomendaciones finales

En este artículo se presentan las conclusiones y las recomendaciones finales del estudio sobre la enfermedad cardiovascular de la mujer en España, realizado por la Sociedad Española de Cardiología. Hay diferencias notables entre mujeres y varones respecto a las características clínicas, el perfil de riesgo, la realización de pruebas diagnósticas, las medidas terapéuticas y el pronóstico en la mayor parte de las enfermedades estudiadas, sobre todo en el síndrome coronario agudo, la insuficiencia cardíaca y la hipertensión arterial. Las diferencias en el manejo diagnóstico y terapéutico son, en general, desfavorables para las mujeres. No existe información adecuada respecto a la fibrilación auricular y las enfermedades valvulares, por lo que es preciso realizar estudios específicos de estas afecciones. Son necesarias campañas de información y educación para concienciar tanto a la sociedad en general como a los profesionales sanitarios sobre estas desigualdades, así como adoptar medidas que contribuyan a mejorar la atención de las enfermedades cardiovasculares en las mujeres.

Palabras clave: Enfermedades cardiovasculares. Prevención. Diferencias por sexo.

and management of cardiovascular disease in Spain over the past 5-10 years. This information comes from population studies and general records of different diseases, obtained in both hospital and outpatient environments using appropriate methodology. Therefore, the results are thought to be representative of the majority of patients with cardiovascular disease in Spain.

The large number of patients included in these studies and registries, and the substantial percentage of

women, allows for reliable analysis of gender differences in the management and characteristics of cardiovascular diseases in Spain with respect to the majority of the most important ailments. The information obtained and presented in this study is exhaustive for the fields of acute coronary syndrome, heart failure, hypertension and heart transplants. There is less information on atrial fibrillation and heart valve diseases.

In general, and across all the diseases, there were important differences according to sex clinical and aetiological characteristics, the cardiovascular risk factor profile, the diagnostic exams and therapeutic measures employed, and the prognosis differed for men and women in most of the pathologies and variables studied. In general, and above all in the field of acute coronary syndrome, women compared unfavourably to men in terms of applying recommended diagnostic measures and therapies, which may affect a worse prognosis. However, even though sex was by itself an independent predictor of some of these differences, it is possible that other variables influence the differences in management and prognosis, such as differences in the initial risk profile and the perception of said risk between women and men, as discussed below.

For acute coronary syndrome (ACS), the study performed represents extensive research on the influence of sex on the characteristics, evolution, management and prognosis of ACS in Spain. It included information from a defined period (1994-2002) for 48,369 patients [13,405 ACS patients with non-ST segment elevation (NSTEMACS)], and 34,334 with ST segment elevation (STEMACS) of which 24.3% were women (26.6% of NSTEMACS patients and 23.2% of those with STEMACS). The study results should be interpreted in light of the limitations escribed in the corresponding section, related to the current validity and potential bias of the methodology used.

Among the NSTEMACS patients, women were older than men (by 6 years in average age) and had a much more unfavourable cardiovascular risk profile, with higher prevalence of hypertension, dyslipidemia and diabetes, although the rate tobacco use of was much lower. In terms of cardiovascular history, the proportion of women with previous cerebral vascular accidents (CVA) or angina was similar to that of men, but men displayed a higher atherosclerotic burden demonstrated by the higher frequency of previous stroke, coronary revascularisation and peripheral artery disease. The use of antiplatelets and antithrombotics in the hospital treatment of patients with NSTEMACS was high, and similar between men and women. In regards to other treatments, the use of beta-blockers was lower in women, a difference that cannot be clearly explained because more intensive

treatment would be expected for patients with these baseline characteristics (higher risk profile). A higher use of angiotensin converting enzyme inhibitors (ACEI) and diuretics was observed in women, probably related to the higher prevalence of hypertension and incidence of heart failure during admission. The mortality and the incidence of adverse events (acute myocardial infarction heart failure and cardiogenic shock) were 50% higher in women, both during the acute phase and during follow-up at 28 days and at 1 year. However, the multivariable analysis showed that sex is a predictive factor independent of hospital mortality even after 28 days. The excess mortality can be explained by other factors frequently associated with female sex such as diabetes, previous myocardial infarction and age.

Among STEACS patients, women presented a different profile than men, similar to the NSTEMACS group although there were some differences. The average age difference was greater in the STEACS group (women were 8.8 years older), but the prevalence of dyslipidemia was similar to the NSTEMACS group. The rest of the differences between men and women were similar to the NSTEMACS group (less prevalence of tobacco users, more hypertension and diabetes, more frequent history of angina and heart failure, and less coronary revascularisation and intermittent claudication in women than in men). The percentage of women with STEACS reperfused with fibrinolysis was lower than the percentage of men. Additionally, the time until reperfusion was longer in women than in men. This resulted from a longer delay both in reaching the hospital (time from onset of pain to admission) and in beginning treatment (time from admission to reperfusion therapy). In women with STEACS, similar to what occurred with NSTEMACS patients, differences were detected in the use of pharmacological interventions and therapeutic resources; considering the higher risk in women, this leads to the suspicion of underuse of these resources for women compared to men. Mortality and hospital complications in women with STEACS were double those of men. As with NSTEMACS, 28-day mortality was very high in patients with STEACS (11.5%) and was twice as high in women (20%) as in men. In contrast to the group of patients with STEACS, being a woman was found to be an independent predictor of hospital mortality at 28 days and at 1 year (increased by 30%).

For heart failure (in studies that included more than 6,000 patients), the prevalence was very high, around 7%, and similar for both women and men. For patients hospitalised for acute heart failure and for stabilised patients monitored during outpatient appointments, women with heart failure were older, had a more unfavourable cardiovascular risk profile (higher prevalence of hypertension and diabetes), less history

of ischemic cardiovascular disease and a distinct aetiology (greater frequency of ischemia in men and of hypertension and other non-ischemic causes in women). Likewise, and likely in relation to this aetiology, the physiopathological type of heart failure was also distinct, with a higher proportion of cases with preserved systolic function in women and of depressed systolic function in men. No big differences were observed in the diagnostic techniques used, except for a higher use of exams to detect myocardial ischemia (ergometry, coronarography) in men. Use of echocardiography to measure ejection fraction was similar in both men and women. No great differences were observed in terms of pharmacological treatment, although the use of ACEI and beta-blockers was slightly, yet significantly, lower among women. Mortality, both in-hospital and long-term, was similar between women and men, although the incidence of readmission for decompensated heart failure was higher in women, which could have been affected by the differences observed in their treatment.

For hypertension, the analysed registries included almost 50,000 patients and concluded that women with hypertension present important differential characteristics compared to men: older age; higher prevalence of obesity, diabetes, hyperlipidemia and metabolic syndrome; lower tobacco use; and differences in target organ involvement (more renal and cerebral vascular alterations, atrial fibrillation and heart failure, and fewer problems related to ischemic cardiovascular disease and peripheral artery disease). No significant differences were observed in the usage of pharmacological treatments, although there was a trend toward higher use of some medications, such as diuretics or nitrates and, above all, non-cardiovascular medication (such as non-steroid anti-inflammatory medication). Blood pressure was not adequately controlled in most of the studied population, and no significant differences were observed between women and men.

There is little information on the prevalence of atrial fibrillation and knowledge of its management characteristics, treatment, prognosis and long-term complications, and it is derived from local rather than national studies. Therefore, it seems necessary to design and perform broad, multicentre studies that include all of Spain. The objectives should be to study its prevalence, both generally and by subgroups of age and sex (epidemiologic al population studies), and to better understand its clinical characteristics, associated diseases, treatments and long-term prognosis (transversal and longitudinal multicentre records).

With respect to heart valve diseases, there are no integral national registries that allow definitive conclusions. Data from the autonomous community of Andalusia indicate that mortality, both from non-rheumatic aortic valve disease and from rheumatic

mitral valve disease, is higher in women than in men at any age. In the Andalusian registry of valve diseases, some sex-related differences were observed in the data: a greater number of hospital admittances among women for severe valve disease and some associated comorbidities such as anaemia; a higher prevalence of rheumatic valve disease in women than in men; and a lower incidence of left ventricular dysfunction in men. In contrast, there were no differences by sex in the use of valve surgeries. As with atrial fibrillation, the lack of national information makes it necessary to design and carry out wider studies.

Finally, in relation to cardiac transplantation, exhaustive data analysis of the National Register of Cardiac Transplantation allows for the extraction of reliable conclusions on sex-related differences in this field (762 women compared with 3,646 men with transplants in Spain from May 1984 to December 2005). The male to female transplant ratio was 5:1. Women were younger (45 ± 18 versus 51 ± 14 years; $p < 0.05$) and had a higher incidence of idiopathic dilated cardiomyopathy (39.8% versus 31.3%; $p < 0.05$) and fewer cardiovascular risk factors (hypertension, 16.2% versus 23.1%; $p < 0.05$; dyslipidemia, 25% versus 36%; $p < 0.05$). Women more frequently had emergency heart transplants (26.8% versus 23.4%; $p < 0.05$) and suffered from acute graft failure (17.4% versus 13.5%; $p < 0.05$). During follow-up, they presented with a higher incidence of bone complications (15.5% versus 10.9%; $p < 0.05$) and lower incidence of dyslipidemia (38% versus 45%; $p < 0.05$), hypertension (36% versus 49%; $p < 0.05$), digestive complications (12% versus 16%; $p < 0.05$) and tumours (9% versus 12.5%; $p < 0.05$). Survival probability was lower in the short term ($p < 0.05$), but similar to men in the medium and long terms ($p = 0.6$). The multivariable analysis showed 14 variables that were associated with mortality in men and only 5 in women. It can be concluded that there are important differences between the number of men and women who received transplants in Spain, which can be partially explained by the lower incidence of ischemic cardiovascular disease at the age when heart transplants are performed; however, other factors probably exist to explain such large differences. The survival probability, except in the early phase, was similar for both sexes.

This report detected differences between men and women in the clinical and demographic profile and in the use of therapeutic resources that explain some of the discrepancy in mortality and morbidity observed in women, which was more evident in more serious occurrences such as heart failure and, above all, in acute coronary syndrome. The higher prevalence of diabetes, hypertension, obesity and concomitant diseases and the total risk profile in women can influence these differences in an important way

because the role of sex by itself is diluted and reduced when multivariable analyses are performed. There are opportunities for improvement that should be highlighted by women-oriented campaigns that raise awareness of ischemic cardiovascular disease, which affects women as dramatically as other diseases already included in the preventive mentality of women, such as breast cancer. On the other hand, programs are needed that change the attitude in all areas of health care to improve the early identification of women with ACS and to optimise treatment in actual practice in accordance with the recommendations of the guidelines from various scientific societies. These programs and campaigns should also place emphasis on the remaining diseases related to ischemic cardiovascular disease, such as heart failure and arterial hypertension, among others.

Some specific recommendations are presented below:

- Campaigns to disseminate the results of the present report both among the general population (general means of communication: printouts, audiovisual and electronics; press conferences, press releases from the Ministry and the Spanish Society of Cardiology, both individually and collectively) and in the scientific community (cardiologists and health professionals in general through news, interviews, and the like in the health-related media, presentations at scientific conferences, publications in scientific magazines, books, pamphlets and others).

- Specific dissemination campaigns at meetings, conferences and generally in contexts specifically related to women. The role of the Observatory of Women's Health of the Ministry of Health and Consumption should be predominant in these campaigns.

- Use of the information obtained in the present report within the strategies of the Ministry of Health and Consumption: internal diffusion, publishing of

monographs, and so on. The discussion of these data would be very interesting in forums where representatives from autonomous health administrations (inter-territorial councils or ad hoc committees) come together with an aim to promote coordinated actions among all the autonomous communities.

- Publishing of a monograph issue of the Spanish Cardiology Journal as a supplement containing the present report findings.

- The design and performance of scientific studies over the coming years in fields where the existing information is scarce and does not cover all of Spain (essentially in the area of atrial fibrillation and valve diseases). In this regard, collaboration between the Ministry of Health and Consumption and the Spanish Society of Cardiology would be of great interest.

- The design and performance of scientific studies over the coming years in the field of ischemic cardiovascular disease, heart failure and hypertension to evaluate the changes produced in the characteristics, management and prognosis of cardiovascular diseases throughout the years. The data obtained with these studies would indicate the effectiveness of the actions taken to improve the care of women with cardiovascular disease in Spain.

- Undertaking a new report on sex-related differences in cardiovascular disease in Spain within 5 years, which would aim to solidify the changes and improvements that have been achieved.

- Finally, the adoption of measures that allow for or facilitate a higher presence of women in clinical studies that evaluate diagnoses or therapeutic measures of different cardiovascular diseases would be of great interest because the participation of women is low in the majority of the available studies upon which most of the current recommendations are based. Health administrations and scientific societies should promote clinical trials and studies specifically designed for women.