

Emergency cardiovascular consultations by women: Is management different in women and men?

ALBA RIESGO GARCÍA

Servicio de Urgencias, Hospital Universitario Central de Oviedo, Asturias, Spain.

CORRESPONDENCE:

Alba Riesgo García
Servicio Urgencias
Hospital Universitario de Asturias.
C/ Celestino Villamil, s/n.
33006 Oviedo, Spain
E-mail: albariesgo@gmail.com

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Cardiovascular diseases, which are the main cause of death in industrialized countries, have traditionally been considered to threaten mainly men. Although the approach to treating women with these diseases has mimicked treatment in men, recent studies have brought to light a number of differences in cardiovascular physiopathology between men and women, in their responses to treatment, and in the attitudes of the medical profession. This review discusses possible gender differences in the management of 4 highly prevalent cardiovascular events that bring patients to the emergency department: chest pain, atrial fibrillation, heart failure, and acute coronary syndrome. [Emergencias 2012;24:325-331]

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Introduction

Cardiovascular disease (CVD) is the leading cause of death in Europe and industrialized countries (43% in men and 54% in women). Coronary disease is the leading cause of death (21% in men and 22% in women); while in men there is a slight downward trend, in women it is increasing¹.

The prevalence of CVD increases with age. In younger age groups, CVD is found predominantly in males, and in more advanced age groups women present CVD more frequently than men. Coronary artery disease appears about 10 years later in women than in men, but the events are more severe and sudden death is more frequent in women². And although the incidence is lower, mortality from CVD is greater in women below 45 years than in men of the same age; over 9,000 women under 45 years suffer an acute myocardial infarction (AMI) event in the U.S. each year and they are twice as likely to die during such events than men³.

Traditionally CVD has been considered an almost exclusively male disease. In the Ebers Papyrus (1500 BC), the clinical symptoms of AMI in a man were described: "If you find a man with cardiac discomfort, with pain in his arms, at the

side of his heart, death is near." This seems to be the trend even today, manifest in the low numbers of women included in studies and trials investigating different cardiovascular diseases. As an example, women account for 50% of the population in studies of arterial hypertension but less than 20% when the object of research is heart failure or arrhythmia⁴. In recent years this has begun to change. From different scientific institutions and societies, the differences in CVD of women are being highlighted. Programs like Go in Red of the American Heart Association or Women at Heart of the European Cardiology Society reflect this. And this has also reached the general population, as evidenced by the fact that it has been on the cover of widely read magazines such as Time.

What is it about women's hearts that makes them different? To understand this we need to go back to concepts of anatomy and physiology. The anatomical reasons are that the female heart, compared to that of men, is smaller, weighs less and has lower muscle mass. At rest, the female heart has lower blood pressure and less volume at the end of diastole, but a higher left ventricle ejection fraction. The right chambers are smaller and have higher ventricular compliance. Loss of

this compliance due to left ventricular hypertrophy, in many cases the consequence of long-standing hypertension, explains the higher incidence of diastolic heart failure (HF) in women. And, to further complicate matters, their coronary arteries are more tortuous and of smaller caliber, making it difficult to carry out therapeutic procedures such as cardiac catheterization and bypass surgery. At the physiological level there are also many differences, mainly due to hormonal factors. Estrogens, whose protective role against arteriosclerotic damage is well known, also influence the expression of L-type calcium channels, increasing the expression of atrial natriuretic factor, which has anti-hypertrophic effects, and also intervene in the renin angiotensin system, preventing and limiting the generation of angiotensin II⁵. All these actions protect the pre-menopausal heart from ventricular hypertrophy and delay the onset of this the most common cause of heart failure in women.

Women and chest pain

Non-traumatic chest pain is a common reason for visits to the emergency department (ED) and health centers, accounting for 11.9% of urgent medical consultations⁶. Of these, 15% are due to acute coronary syndrome (ACS) diagnosed clinically and by electrocardiography (ECG), increasing to 35% when including ACS with normal initial ECG. The initial clinical assessment of chest pain has always been difficult in the ED and is even more complex in women. Women more frequently present atypical chest pain, with increased prevalence of less common causes of chest pain such as vasospasm or microvascular angina, as well as non-ischemic syndromes like mitral valve prolapse⁷.

Very few studies have evaluated ED management of chest pain in women. Most data on initial action are drawn from work whose objective was the analysis of management during hospitalization. In Spain, recent research carried out in a structured chest pain unit (CPU) belonging to an ED found some gender differences in the initial management of chest pain: it took longer to perform women's admission ECG, significantly so in the group of patients without electrocardiographic or enzymatic abnormalities, but with pain suggestive of ACS. Furthermore, women less often had treadmill stress tests requested by ED attending physicians to clarify the diagnosis, but these differences could be explained by the older age of

women and, therefore, their functional limitations and greater difficulties for undergoing such a test⁸.

A Canadian study concluded that women attending emergency services for chest pain, stable/unstable angina or AMI were discharged directly from the ED more often than men, and underwent fewer revascularization procedures⁹. The creation of CPUs in hospital EDs with protocols for initial urgent attention of non-traumatic chest pain would help minimize these gender differences in care and ensure equity^{6,8}.

Women and atrial fibrillation

Atrial fibrillation (AF) is a very frequent type of arrhythmia¹⁰, and potentially serious with high morbidity and double the mortality rate of patients who suffer HF and arterial thromboembolic disease^{11,12}. AF involves high health costs per se and for its complications, represents the most common arrhythmia in outpatient and emergency services, and underlies about 10% of hospital admissions^{11,13}. All this could be prevented or controlled with early treatment of the arrhythmia.

The prevalence of AF increases with age¹⁴: it affects 0.4% of the general population, 3-5% of people aged ≥ 65 years and more than 9% of those over 80 years^{11,15}. The risk of AF and the overall prevalence of the disease are similar in women and men; although prevalence is greater in men¹⁶, the overall figures are equal due to greater life expectancy in women¹⁷. In addition, the course of AF in women is worse, with significant differences in the clinical severity of stroke secondary to AF, hospital mortality and disabling sequelae.

These features are reflected in the Euro Heart Survey on Atrial Fibrillation (EHS-AF)¹⁸, involving 5,333 patients, where women participants (42% of the total) were characterized as older and with more cardiovascular comorbidity (Table 1). The ATRIA study (2009) of 13,559 AF patients focused on the benefits of oral anticoagulation with warfarin. It concluded that women with AF had, in the absence of anticoagulant therapy, higher embolic risk than men (3.5% versus 1.8%) in all age groups and that oral anticoagulation with warfarin was at least as effective, if not more, in women as in men¹⁹. AF per se increases mortality by 1.5 in men and 1.9 in women²⁰.

In a Spanish study conducted at different levels of care (primary care, ED, outpatient cardiology and hospitalization), certain gender differences

Table 1. Risk factors and morbidity associated with atrial fibrillation in the EHS-AF¹⁸

	Women	Men	P
Age in years (mean \pm SD)	70 \pm 12	64 \pm 13	< 0.001
Heart failure (%)	35	33	NS
Ischemic heart disease (%)	30	36	< 0.001
Valvular heart disease (%)	15	7	< 0.001
Diabetes (%)	21	16	< 0.001
Hypertension (%)	69	60	< 0.001
Previous stroke (%)	7	5	< 0.01

EHS-AF: Euro Heart Survey on Atrial Fibrillation. SD: standard deviation.

were observed in the management of AF. Briefly, women were more frequently prescribed digoxin, underwent cardioversion less often and were referred to cardiologists less often²¹. Analysis of the results adjusted for age and Barthel index, two possible confounding factors since women with AF are older and more dependent, differences in the treatment of AF persisted, and the study confirmed that a more conservative approach was adopted in female patients (Table 2). This has been attributed to underestimating the importance of the age factor in AF and women's delayed arrival at cardiology clinics. Similar results, i.e. more frequent treatment with digoxin²² and less with beta blockers in the case of women¹⁸, have been reported.

The CARDIOTENS study²³ reported a higher prevalence of AF and greater comorbidity in women, with more frequent cases of HF or ischemic events. The study also found that women were referred less frequently to a cardiologist than men. This result agrees with that of Roten et al²⁴ where women with AF were three times less often referred to a cardiologist than men with AF.

More intense therapeutic measures are needed in women with AF. The presence of this arrhythmia increases all-cause cardiovascular and non-cardiovascular morbidity and mortality as from the first episode²⁵, and especially fatal and nonfatal stroke, even more than in men²⁶. Once

Table 2. Gender differences in the management of patients with atrial fibrillation

	Women	Men	P
EHS-AF (2007) ¹⁸			
OAC therapy (%)	65	65	NS
Digoxin (%)	30	25	< 0.001
Cardioversion (%)	22	28	< 0.001
Catheter ablation (%)	3	6	< 0.001
Riesgo et al (2011) ²¹			
OAC therapy (%)	63	65	NS
Digoxin (%)	58	45	< 0.01
Cardioversion (%)	9	16	< 0.01
Catheter ablation (%)	1.4	3.5	NS

EHS-AF: Euro Heart Survey on Atrial Fibrillation. OAC: Oral anticoagulation.

persistent AF is established, aggressive treatment and control of heart rate is required to decrease morbidity and mortality²⁷ as well as anticoagulation sustained within the therapeutic range. In under-treated women, the risk of embolism is higher than in males¹⁹, and the risk of bleeding due to overdose of anticoagulant therapy is also higher in women than in men²⁸.

Women and heart failure

HF is associated with high morbidity and mortality, and is a leading cause of hospitalization in developed countries. In Europe, with a population of over 900 million people, the European Society of Cardiology (ESC) estimates that over 15 million people suffer this disease, which is asymptomatic in 4% of patients. The prevalence increases markedly with age to over 10% in the age group 70 to 80 years, and the prognosis is poor since 50% of HF patients die within 4 years after diagnosis. Furthermore, of those who are hospitalized for acute HF, 40% die or are re-admitted in the following year²⁹. The prevalence of HF in Spain is high, around 7-8% in the general population and 16% in people over 75 years of age³⁰.

Men and women with AF present different clinical characteristics, in part due to different etiology. Women who are hospitalized for AF are older, more frequently diabetic, and present hypertensive etiology more often than men while ischemic etiology is less frequent than in men. In addition, women present preserved ejection fraction more frequently than men^{31,32}. These differences in etiology are important in terms of prognosis. Thus, the Framingham study³³ observed that women with HF had better prognoses than men, a fact corroborated by the BEST study³⁴, which showed that this was due to a lower incidence of coronary artery disease and higher prevalence of preserved systolic function in women.

Several studies have addressed gender differences in hospital management of patients with HF. The Euro Heart Survey on Heart Failure (EHS-HF)³⁵ in about 8,914 European patients with heart failure showed that women with HF were older than men, had a higher prevalence of hypertension, diabetes, and valvular heart disease than men, a higher percentage of preserved systolic function and a lower prevalence of ischemic heart disease. In this study, ventricular function in women was evaluated less frequently; they less often received treatment with angiotensin convert-

ing enzyme inhibitors (ACEI), beta-blockers or spironolactone, and digoxin was more often prescribed for women. Finally, women with HF were admitted to hospital cardiology wards less often than men. In Spain, the ATTICA study³⁶ found no gender differences in coronary angiography or echocardiographic ejection fraction measurement, nor in the recommendations on general and non-pharmacologic measures, but there were gender differences in the drug prescribed at discharge: fewer women were prescribed beta-blockers and ACEIs than men.

Regarding the management of acute HF in the ED, the ADHERE study³⁷ showed that American women were more often admitted for exacerbation of HF than American men, and that these women were older, with a higher prevalence of hypertension and diastolic dysfunction and less ischemic heart disease and systolic dysfunction with respect to men. A Spanish study within the EAHFE project (Epidemiology of Acute Heart Failure in Emergency services) confirmed these data: female patients were older and had a higher prevalence of risk factors and comorbidity³⁸ (Table 3). Paroxysmal nocturnal dyspnea and orthopnea were the predominant symptoms while lower limb edema and basal crackles were the most consistent signs, but there were no apparent gender differences. In assessing the acute treatment of HF, no gender differences were observed: all patients were treated as recommended by international guidelines, with oxygen in different regimes according to need, and diuretics to relieve pulmonary congestion. There were differences in treatment: more male patients received beta blockers and more female patients received digoxin therapy. These differences could be explained by the different precipitating cause of worsening HF: in men it was predominantly ischemic and in women it was AF. In addition, women were less often assessed by cardiologists or admitted to the cardiology department; they were more often admitted to internal medicine, and these data match those of the EHS-HF³⁵ and ADHERE³⁷ studies.

Women and non-ST elevation acute coronary syndrome

Acute coronary syndrome (ACS) is one of the diseases in which most gender management differences exist. As mentioned, the atypical characteristics of ACS presentation in women, with less frequent chest pain so typical in men³⁹, could account for some of these differences⁴⁰⁻⁴².

Table 3. Gender differences in risk factors, morbidity, treatment and destination of patients with heart failure

	Women	Men	P
EHS-HF (2008) ³³			
Age in years (mean ± SD)	74.4 ± 11.9	68.3 ± 12.7	< 0.001
Hypertension (%)	59	49	< 0.001
DM (%)	29	26	< 0.001
Ischemic heart disease (%)	56	66	< 0.001
Atrial fibrillation (%)	46	42	< 0.001
Preserved systolic function (%)	41	23	< 0.001
Beta-blocker therapy (%)	32	41	< 0.001
Treatment with ACE inhibitors (%)	60	69	< 0.001
Treatment with diuretics (%)	88	85	NS
Admitted to cardiology (%)	36	53	< 0.001
Admitted to internal medicine (%)	55	46	< 0.001
ATTICA (2008) ³⁴			
Beta-blocker therapy (%)	74.5	83.7	< 0.001
Treatment with ACE inhibitors (%)	83.5	91.4	< 0.01
Treatment with diuretics (%)	98	98	NS
ADHERE (2006) ³⁵			
Age in years (mean ± SD)	74.5	70.1	< 0.001
Ischemic Heart Disease (%)	51	64	< 0.01
Hypertension (%)	76	70	< 0.01
Preserved systolic function (%)	51	28	< 0.001
EAHFE (2011) ³⁹			
Age	79.7	75.6	< 0.001
Hypertension (%)	83.4	74.9	< 0.01
DM (%)	42.9	42.4	NS
Ischemic heart disease (%)	26.5	43.3	< 0.001
Preserved systolic function (%)	49.4	28	< 0.001
Beta-blocker therapy (%)	19.6	30.2	< 0.001
Treatment with ACE inhibitors (%)	33.7	42.1	< 0.05
Treatment with diuretics (%)	62.9	66.6	NS
Admitted to cardiology (%)	8	13.8	< 0.001
Admitted to internal medicine (%)'	26.2	25.8	NS

DM: diabetes mellitus, ACE inhibitors: angiotensin converting enzyme inhibitors. SD: standard deviation.

Women take longer in seeking emergency medical attention and this delay has been reported for all types of ACS^{43,44}. Different reasons have been advanced to explain this, including greater age and more frequent atypical symptoms, but none seem satisfactory. Perhaps, as Sanchez says, the most important is that women do not perceive the situation as life threatening⁴⁵.

Only two studies address gender differences in the initial management of ACS in Spanish EDs (Table 4). One analyzed urgent attention in the case of ST-elevation ACS⁴⁶ and found no differences in the treatment administered by hospital and out-of-hospital emergency departments, but did note delays in attending women, both in symptom onset – hospital arrival time and symptom onset – admission ECG time. The other study analyzed attention in cases of non-ST elevation ACS⁴⁷ and noted that the women attending the ED for this condition were older than the men and had a higher prevalence of hypertension, diabetes mellitus, obesity and previous HF, although the latter was not significantly different, and there were fewer smokers in the female patient group;

Table 4. Differences in cardiovascular risk factors, times and treatment in ST-elevation ACS⁴⁴ and non-ST-elevation ACS⁴⁵

	ST-elevation ACS			non-ST-elevation ACS		
	Women	Men	P	Women	Men	P
Age in years (mean ± SD)	71.7 ± 10.5	62.3 ± 12.3	< 0.001	76 ± 11	67 ± 13	< 0.001
Hypertension (%)	48.1	66.7	< 0.05	81.1	63.5	< 0.001
Diabetes mellitus (%)	37	21.9	< 0.005	50.3	30.4	< 0.001
Smoking (%)	18.5	58.1	< 0.001	9.1	34.1	< 0.001
Door-to-ECG (minutes) (mean ± SD)	13	6.4	< 0.01	22	16	NS
Symptom onset-hospital arrival (minutes) (mean ± SD)	503.3	240.3	< 0.05	306	258	NS
ASA	93	96	NS	77.1	74.6	NS
Fibrinolysis/PTCA	25.1	22.1	NS			
Cardiac catheterization				29.7	40.7	< 0.05

ACS: acute coronary syndrome, ECG: electrocardiogram; SD: standard deviation; ASA: acetylsalicylic acid.

these results are in agreement with those of previous studies^{40-42,46,47}. Women with non-ST elevation ACS arrived later at Spanish EDs than men. Despite this, the treatment administered at both hospital and out-of-hospital emergency services did not differ according to gender. Women with acute myocardial infarction, with or without ST elevation, are less frequently admitted to intensive care or coronary units than men and undergo fewer interventional procedures, in agreement with many European and American studies^{40-42,46}. Several reasons for this difference have been proposed: later arrival at the hospitals by women means the time window for safe performance of invasive procedures is often exceeded; their lower probability of three-vessel disease and LV dysfunction together with greater comorbidity and worse clinical condition makes invasive cardiac procedures more risky^{48,49}. Although the prevalence of coronary heart disease is lower in women than in men and occurs approximately ten years later, we should remember that female patient mortality rate is higher². We need to improve the care of ACS in women to reduce this.

Conclusions

There are anatomical and physiological reasons that may explain the different etiology of coronary disease in women as compared to men, but this does not justify the difference in healthcare. Women must be included in all future aspects of biomedical research, as promoted by the American National Institute of Health, to define these gender differences and incorporate these results into clinical practice for the prevention, diagnosis and treatment of heart disease in women. It may not be unreasonable to posit the need for different treatment guidelines for the same pathology depending on the gender of the patient. This

seems to be the line taken by the American Heart Association with their recent guideline update on prevention of CVD in women⁴⁹. As renowned cardiologist Dr. Nanette Wenger has noted: "It is time medical science abandoned the 'bikini' view of women, with its focus on breast cancer and gynecological and obstetric problems."

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Manejo clínico de las mujeres que consultan en urgencias por patología cardiovascular: ¿existen diferencias respecto a los hombres?

Riesgo García A

Las enfermedades cardiovasculares son la primera causa de mortalidad en los países industrializados y tradicionalmente han sido consideradas una patología predominantemente masculina. Las mujeres con enfermedad cardiovascular han sido tratadas siempre a imagen y semejanza de los varones, pero en los últimos años diferentes estudios han puesto de manifiesto la existencia de notables diferencias tanto en la fisiopatología de la enfermedad como en la respuesta a los tratamientos y en la actitud de los profesionales ante estas patologías. En este artículo se revisan las posibles diferencias que existen en cuanto al manejo, en función del género del paciente, de cuatro problemas cardiovasculares muy prevalentes en los servicios de urgencias: el dolor torácico, la fibrilación auricular, la insuficiencia cardíaca y el síndrome coronario agudo. [Emergencias 2012;24:325-331]

Palabras clave: Enfermedades cardiovasculares. Servicio de urgencias. Dolor torácico. Fibrilación auricular. Insuficiencia cardíaca. Síndrome coronario agudo.