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Original article

Sex-based Differences in Clinical Features, Management, and 28-day and 7-year Prognosis of First Acute Myocardial Infarction. RESCATE II Study

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ABSTRACT

Introduction and objectives: To analyze sex-based differences in clinical characteristics, management, and 28-day and 7-year prognosis after a first myocardial infarction.

Methods: Between 2001 and 2003, 2042 first myocardial infarction patients were consecutively registered in 6 Spanish hospitals. Clinical characteristics, management, and 28-day case-fatality were prospectively recorded. Seven-year vital status was also ascertained by data linkage with the National Mortality Index.

Results: The registry included 449 women and 1593 men with a first myocardial infarction. Compared with men, women were older, had a higher prevalence of hypertension and diabetes, and were more likely to receive angiotensin-converting enzyme (ACE) inhibitors but were less likely to receive beta-blockers or thrombolysis. No differences were observed in use of invasive procedures. More women had non-ST-segment elevation and unclassified myocardial infarction than men (37.9% vs 31.3% and 9.8% vs 6.1%, respectively; both $P<.001$). Case-fatality at 28 days was similar in women and men (5.57% vs 4.46%; $P=.39$). After multivariate adjustment, the odds ratio of 28-day mortality for men was 1.06 (95% confidence interval: 0.49-2.27; $P=.883$) compared with women. After multivariate adjustment, men had higher 7-year mortality than women, hazard ratio 1.93 (95% confidence interval: 1.46-2.56; $P<.001$).

Conclusions: There are demographic and clinical differences between men and women with a first myocardial infarction. The short-term prognosis of a first myocardial infarction in this century is similar in both sexes. However, the long-term vital prognosis after a first myocardial infarction is worse in men than in women. These results are observed in both ST-segment elevation myocardial infarction and non-ST-segment elevation myocardial infarction events.

Diferencias en función del sexo en las características clínicas, tratamiento y mortalidad a 28 días y 7 años de un primer infarto agudo de miocardio. Estudio RESCATE II

Palabras clave:
Infarto agudo de miocardio
Pronóstico según sexo
Sexo

RESUMEN

Introducción y objetivos: Analizar las diferencias en función del sexo en las características clínicas, tratamiento y mortalidad a los 28 días y a los 7 años de un primer infarto de miocardio.

Métodos: Entre 2001 y 2003, 2.042 pacientes con un primer infarto de miocardio ingresaron consecutivamente en seis hospitales españoles. Se recogen prospectivamente las características clínicas, el tratamiento y la mortalidad a los 28 días. Se dispone del estado vital a los 7 años mediante consulta del Índice Nacional de Defunciones.

Resultados: Se incluyó a 449 mujeres y 1.593 varones con un primer infarto de miocardio. En comparación con los varones, las mujeres eran mayores y tenían mayor prevalencia de hipertensión y diabetes mellitus; también recibieron más tratamiento con inhibidores de la enzima de conversión de la angiotensina, pero menos bloqueadores beta y trombolisis. No hubo diferencias en el uso de procedimientos invasivos. Las mujeres tuvieron más infartos de miocardio sin elevación del segmento ST o no clasificables (el 37,9 frente

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al 31,3% y el 9,8 frente al 6,1% respectivamente; p < 0,001). La mortalidad a los 28 días era similar en mujeres y varones (el 5,57 y el 4,46%; p = 0,39). Tras el ajuste multivariable, la *odds ratio* de mortalidad a los 28 días de los varones fue 1,06 (intervalo de confianza del 95%, 0,49-2,27; p = 0,883). Los varones tuvieron mayor mortalidad a los 7 años que las mujeres (*hazard ratio* = 1,93; intervalo de confianza del 95%, 1,46-2,56; p < 0,001).

Conclusiones: Hay diferencias clínicas y demográficas entre varones y mujeres que ingresan por un primer infarto de miocardio. El pronóstico a corto plazo es similar en ambos sexos. La mortalidad a 7 años de un primer infarto de miocardio es peor en varones que en mujeres. Estos resultados se observan en infartos agudos de miocardio con y sin elevación del segmento ST.

Abbreviations

AMI: acute myocardial infarction
NSTEMI: non-ST-elevation myocardial infarction
STEMI: ST-segment elevation myocardial infarction

INTRODUCTION

During the last 3 decades a large number of studies have focused on the differences between men and women in ischemic heart disease characteristics.[1,2] One of the main areas of research has been the differences between the sexes in ischemic heart disease prognosis. Women have a worse short-term prognosis after an acute myocardial infarction (AMI) in most of these studies [3–12] but not in all.[13] This poorer short-term prognosis has been mainly observed in ST-segment elevation myocardial infarction (STEMI) cases, particularly in younger women, and seems to be attenuated with age.[14] In other studies, the worse prognosis of AMI in women was mainly related to higher age and comorbidity and to differences between the sexes in the pathophysiology[15–17] and clinical presentation of the disease,[15,18–20] as well as to a lower use of effective drugs and procedures during the acute phase of the disease in women.[15,21–26] However, this mortality gap has been decreasing.[27]

A few studies have analyzed differences between sexes in long-term prognosis after AMI, with conflicting results. Compared with men, women have been reported to have better,[28,29] worse,[30,31] and similar long-term prognosis.[13,32–35]

We reported that in the 1990s women had more lethal first AMI than men regardless of age and comorbidity.[12] The present study had 3 aims: to determine whether this difference persisted in the first decade of the 21st century, whether there are differences between men and women in 1-year and 7-year mortality after a first AMI and, if so, whether these differences are present in both STEMI and non-ST-segment elevation myocardial infarction (NSTEMI)

METHODS

Study Design

This is a prospective register of patients with a first AMI undertaken in 6 public hospitals in Spain, with a long-term follow-up of vital status. All patients over 18 years of age who were admitted with a first AMI within 72 h of symptom onset from September 2001 to June 2003 were prospectively and consecutively included.

The study was approved by the local ethics committee and all participants were informed and provided signed consent.

Study Population

The diagnosis followed the European Society of Cardiology/American College of Cardiology (ESC/ACC) definition[36] that AMI is a myocardial necrosis secondary to ischemia. Myocardial necrosis is defined as elevated levels (according to the normal levels as defined in each center) of troponin T or I, or of the creatine phosphokinase-MB fraction, in the presence of symptoms related to myocardial ischemia. Exclusion criteria were a history of previous AMI, residence outside the center's catchment area, and serious illness unrelated to the admission episode that limited the patient's life expectancy.

Variables of Interest

A standardized questionnaire administered by trained personnel was used to prospectively gather demographic variables and comorbidities. History of classical risk factors was based on previous diagnosis or treatment or de novo diagnosis during hospital stay using the following criteria: hypertension (systolic blood pressure greater than or equal to 140 or diastolic blood pressure greater than or equal to 90 mmHg), diabetes (2 fasting glucose determinations greater than or equal to 126 mg/dL or 1 glucose determination greater than or equal to 200 mg/dL), dyslipidemia (low-density lipoprotein cholesterol greater than 160 mg/dL or high-density lipoprotein cholesterol lower than 35 in men, or 45 mg/dL in women). Information related to previous smoking and angina was also recorded by self-report.

Clinical characteristics of the event were recorded, including the delay between symptom onset and hospital monitoring, AMI location, presence of ST-segment elevation on the admission electrocardiogram, appearance of Q waves, and complications such as the development of pulmonary edema or cardiogenic shock or the presence of malignant ventricular arrhythmias within the first 48 h (defined as the appearance of ventricular fibrillation or sustained ventricular tachycardia requiring immediate medical attention). Finally, management of the acute event was recorded, including pharmacological treatments during hospital stay and at discharge, reperfusion (thrombolysis or primary percutaneous coronary intervention), and other procedures such as pharmacological or stress-testing techniques to assess the presence of ischemia, echocardiography, coronary angiography to determine the number of vessels with severe lesions, and elective surgical or percutaneous coronary revascularization.

Each participating hospital followed its own protocols for the clinical management of the patients. All of the hospital protocols followed national and international clinical practice guidelines in force at the time of the study.[36–38]

Events of Interest

Events of interest were defined as 28-day, 1-year, and 7-year mortality, with a follow-up of vital status until December 31, 2009. An individual follow-up was performed in all patients (most of them with a clinical visit and the rest by phone call) to assess 28-day events (angina, reinfarction, stroke, death). Fatal cases were identified through access to the Spanish National Death Registry, an exhaustive and mandatory official database collecting individual