

# In-Hospital and Long-Term Mortality in Women With Acute Myocardial Infarction Treated by Primary Angioplasty

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**Introduction and objectives.** Mortality and morbidity after ST-elevation myocardial infarction (STEMI) are higher in women than men. It is not clear whether reperfusion by elective treatment with primary angioplasty can improve the poor prognosis in women with this condition. The objective of this study was to determine the effect of sex on clinical characteristics, and on in-hospital and long-term outcomes in patients with STEMI undergoing reperfusion by primary angioplasty.

**Methods.** A prospective observational study was performed in 838 consecutive patients with STEMI treated by primary angioplasty at a single hospital. Of these, 183 (22%) were women.

**Results.** Women were older (70 years vs 62 years;  $P < .01$ ), were less frequently smokers (8% vs 53%;  $P < .01$ ), more frequently had diabetes (45% vs 27%;  $P < .01$ ) or hypertension (59% vs 36%;  $P < .01$ ), presented later for angioplasty (4.1 h vs 3.6 h;  $P = .05$ ), and experienced cardiogenic shock more frequently during the procedure (21% vs 12%;  $P < .01$ ). There were no differences in the culprit vessel most often responsible for the infarction, in the procedural success rate, or in stent or glycoprotein IIb/IIIa inhibitor use. The total in-hospital mortality rate was higher in women (22% vs 9%;  $P < .01$ ), as was the adjusted in-hospital rate (odds ratio 2.5, 95% confidence interval 1.2-5.2). During long-term follow-up after discharge (median 35.4 months), there was no significant difference in age-adjusted survival rate (relative risk 1.2, 95% confidence interval 0.7-1.9).

**Conclusions.** Despite recent advances in the treatment of STEMI, women experience greater in-hospital mortality, even after adjustment for baseline clinical characteristics. However, the long-term age-adjusted mortality rate in women discharged from hospital was similar to that in men.

**Key words:** Sex. Women. Myocardial infarction. Primary angioplasty.

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## Mortalidad a corto y largo plazo en mujeres con infarto de miocardio tratado con angioplastia primaria

**Introducción y objetivos.** Las mujeres presentan, con respecto a los varones, una mayor mortalidad y morbilidad tras un infarto agudo de miocardio con elevación del segmento ST (IAMEST). Hay controversia sobre si la angioplastia primaria (ACTPp) como tratamiento de elección logra contrarrestar el peor pronóstico de las mujeres en esta situación. El objetivo fue determinar la influencia del sexo en las características clínicas y en el pronóstico intrahospitalario y a largo plazo de un grupo de pacientes con IAMEST tratados con ACTPp como método de reperusión.

**Métodos.** Estudio observacional prospectivo de una cohorte de 838 pacientes consecutivos, de ellos 183 (22%) mujeres, con IAMEST tratados con ACTPp en un único centro.

**Resultados.** Las mujeres fueron mayores (70 frente a 62 años;  $p < 0,01$ ), menos fumadoras (el 8% frente al 53%;  $p < 0,01$ ), más diabéticas (el 45 frente al 27%;  $p < 0,01$ ), hipertensas (el 59 frente al 36%;  $p < 0,01$ ), se presentaron con mayor retraso (el 4,1 frente al 3,6 h;  $p = 0,05$ ) y más shock cardiogénico durante el procedimiento (del 21 frente al 12%;  $p = 0,01$ ). No hubo diferencias en la arteria causante del IAM, en el éxito angiográfico o en el uso de *stents* o inhibidores de la glucoproteína IIb/IIIa. La mortalidad intrahospitalaria fue mayor en las mujeres, tanto en el análisis bruto (el 22 frente al 9%;  $p < 0,01$ ) como en el multivariable (*odds ratio* = 2,5; intervalo de confianza [IC] del 95%, 1,2-5,2). En el seguimiento clínico a largo plazo (mediana de 35,4 meses) no hubo diferencias en los supervivientes tras el alta tras ajustar por la edad (riesgo relativo = 1,2; IC del 95%, 0,7-1,9).

**Conclusiones.** A pesar de los recientes avances en el tratamiento del IAMEST, las mujeres presentan una mayor mortalidad hospitalaria ajustada por características basales. Las mujeres supervivientes tras el alta hospitalaria tuvieron una similar mortalidad a largo plazo cuando se ajustó por la edad.

**Palabras clave:** Sexo. Mujeres. Infarto de miocardio. Angioplastia primaria.

## INTRODUCTION

Cardiovascular disease is one of the main causes of death in women in Western countries.<sup>1-3</sup> The unadjusted

## ABBREVIATIONS

STEMI: ST-segment elevation myocardial infarction.

mortality associated with ST-segment elevation myocardial infarction (STEMI) is higher in women than men, irrespective of treatment with thrombolysis.<sup>4</sup> The greater mortality in women may be partially explained by increased age, the presence of a greater number of cardiovascular risk factors, less use of diagnostic procedures, less aggressive treatment in women, or sex differences in the biologic response to infarction.

Compared with thrombolysis, treatment of STEMI by mechanical reperfusion has been shown to improve prognosis in terms of survival, reinfarction, and hemorrhagic complications.<sup>5</sup> In recent years, the use of new devices, such as stents, and the development of new antiplatelet drugs have led to improvements in the results obtained with the technique.<sup>6</sup>

Following introduction into clinical practice of the current treatments for STEMI, there is a lack of consensus on whether sex is an independent factor associated with mortality following adjustment for cardiovascular risk factors.<sup>6-9</sup> It remains unclear whether or not primary angioplasty can improve the worse prognosis presented by high-risk groups, such as women with STEMI.

The aim of this study was to assess the clinical characteristics and in-hospital survival of women with STEMI treated by primary angioplasty compared with those of men following adjustment for cardiovascular risk factors and other variables associated with prognosis. The secondary objectives of the study were to assess long-term mortality, repeat hospital admission for cardiovascular causes, and repeat revascularization.

## METHODS

The data presented correspond to the registry of percutaneous interventional procedures for the treatment of STEMI in the region of Murcia, Spain.<sup>10</sup> Baseline characteristics and cardiac events were prospectively registered from 2000 to 2003, inclusive, in all patients undergoing primary angioplasty for STEMI in a tertiary hospital. The tertiary referral hospital is situated in the geographic center of the region, performs a high volume of coronary interventional procedures, and has a cardiologist and catheterization team on call at all times.

### Patients

The registry included patients with STEMI, defined as symptoms compatible with myocardial ischemia of more than 30 minutes' duration or that persisted after

administration of nitrites, and persistent ST-segment elevation in the electrocardiogram (ECG) of more than 1 mm in 2 contiguous leads or nondiagnostic ECG (complete left bundle-branch block [LBBB] or pacemaker rhythm). The window for treatment by primary angioplasty was taken as the 12 hours following onset of symptoms, unless symptoms or signs of myocardial ischemia persisted. Patients were excluded if they had received thrombolytic therapy for the current infarction in the 24 hours prior to the procedure. Patients who attended the referral hospital for percutaneous interventional treatment were systematically treated by primary angioplasty. The decision to refer patients from other hospitals in the region for mechanical reperfusion was made by the physician responsible for their treatment. Following the procedure, the patients were returned to their referring hospital in a mobile intensive care ambulance if their condition allowed or at the discretion of the attending interventional cardiologist. Following discharge, clinical follow-up was performed by personal or telephone interview, or review of medical reports.

### Procedure

In all patients included in the study, mechanical reperfusion of the artery responsible for the infarction was attempted. Other arteries were treated when considered appropriate by the attending interventional cardiologist or in the case of cardiogenic shock. The approach, material used, medication administered, and additional procedures (orotracheal intubation, intraaortic balloon pump, temporary pacemaker) were decided by the attending interventional cardiologist. Cardiogenic shock in the catheterization laboratory was defined as the presence of a sustained systolic blood pressure of less than 90 mm Hg or the need for pharmacologic or mechanical support to maintain blood pressure and cardiac output. Angiographic success was defined as Thrombolysis in Myocardial Infarction (TIMI) III flow with residual stenosis of less than 20% and the absence of major complications.

### Statistical Analysis

Continuous variables are shown as means (SD) and were compared by Student *t* test for independent samples. Categorical variables were compared by Fisher's exact test. Statistical significance was established as a bilateral value of  $P < .05$  or a confidence interval (CI) that did not include 1.0. Logistic regression was used to assess the effect of sex on in-hospital mortality, using an initial model containing age, time to treatment, smoking, diabetes, cardiogenic shock, culprit artery, number of vessels, prior ischemic heart disease, prior heart surgery, ventricular fibrillation, hypertension, prior stroke, and the interaction of those variables with sex. Dummy

variables were used for analysis of the variable “number of vessels” and the reference category was single-vessel disease. When no significant interactions were observed with the chunk test, the model was simplified by elimination of confounding variables that did not cause substantial changes in the relationship between sex and the event. Stepwise elimination was used to select variables predictive of in-hospital mortality. The models were calibrated according to the Hosmer and Lemeshow goodness-of-fit test. Multivariate analysis of long-term events was performed with a Cox proportional hazards model including the variables sex and age.

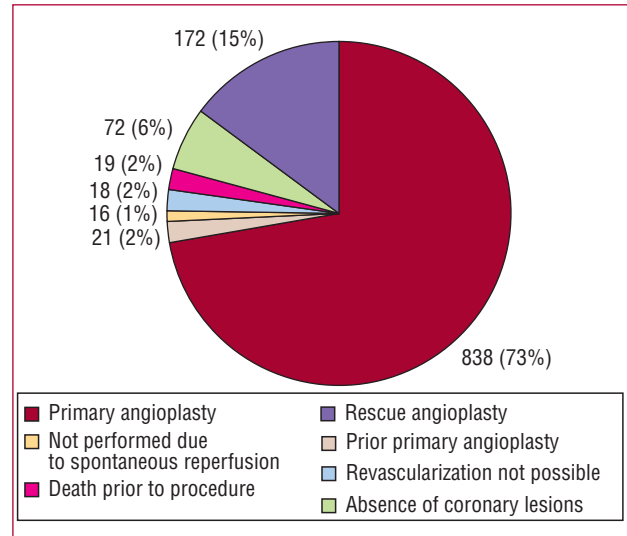
## RESULTS

### Population

During the 4 years covering the inclusion period, 1156 urgent percutaneous coronary procedures were indicated for treatment of STEMI. Of those, thrombolytic therapy had been provided in the previous 24 hours in 172 (15%) patients and in another 113 (10%) the procedure was not performed for other reasons (Figure 1); those patients were therefore excluded from the study. Finally, 838 patients were included in the analysis, of which 655 (78%) were men and 183 (22%) women.

### Baseline Patient Characteristics and Characteristics of the Procedures

The baseline characteristics of the patients according to sex are shown in Table 1. The group of women was older, contained more individuals who were hypertensive or diabetic, included fewer smokers, and had a higher proportion of individuals with a history of cerebrovascular disease. The characteristics of the procedure are shown in Table 2. Women arrived in the catheterization laboratory with a longer delay from onset of symptoms and a larger percentage of women had delays of at least 6 hours (20% vs 13% in women and men, respectively;  $P=.03$ ). The patient group contained 47% of individuals who had been referred from other hospitals for mechanical reperfusion treatment; the number of women referred from other hospitals was proportionally lower. No differences were observed in terms of the artery responsible for the infarction but a tendency towards a greater number of diseased vessels was observed in women. During the procedure, women presented greater hemodynamic instability (hemodynamic shock in the catheterization laboratory of 21% compared with 12% in men;  $P<.01$ ) and more often required a temporary pacemaker. A tendency was observed towards a lower number of episodes of malignant ventricular arrhythmia requiring electrical cardioversion in women. No differences were seen in the use of stents or glycoprotein IIb/IIIa inhibitors, or in terms of procedural success.



**Figure 1.** Procedures employed in acute myocardial infarction with ST-segment elevation.

### In-Hospital Mortality

Greater in-hospital mortality was observed in women than men (21.5% vs 8.6%,  $P<.01$ ; Figure 2). There was a higher in-hospital mortality in the subsets of women with cardiogenic shock and women aged more than 75 years (Figure 3). No sex differences were observed in the subset of patients under 75 years old who did not have cardiogenic shock (4.1% vs 2.1%,  $P=.27$ ). When analyzed according to the number of vessels affected, mortality was higher in women, although significant differences were only observed in patients with single-vessel disease. Likewise, women displayed greater in-hospital mortality irrespective of the site of the infarction (Figure 4). The differences were maintained following adjustment for confounding variables (Table 3). Predictors of in-hospital mortality according to sex in the univariate and multivariate analysis are shown in Tables 4 and 5.

**TABLE 1. Baseline Clinical Characteristics\***

	Total	Men	Women	P
Patients	838	655 (78%)	183 (22%)	
Age, y	63.3 (12)	61.5 (12)	69.6 (12)	<.01
BMI	28 (4)	28 (4)	28 (5)	.16
Diabetes	261 (31%)	178 (27%)	83 (45%)	<.01
Hypertension	344 (41%)	236 (36%)	108 (59%)	<.01
Dyslipidemia	239 (29%)	179 (28%)	60 (33%)	.17
Smoking	364 (43%)	349 (53%)	15 (8%)	<.01
Previous CVS	15 (2%)	14 (2%)	1 (1%)	.21
Previous CVA	48 (6%)	32 (5%)	16 (9%)	.07
Prior ischemic heart disease	143 (17%)	114 (17%)	29 (16%)	.66

\*Data are shown as means (SD) or number of patients (%). BMI indicates body mass index; CVS, cardiovascular surgery; CVA, cerebrovascular accident.

**TABLE 2. Characteristics of the Procedure According to Sex\***

	Total	Men	Women	P
Treatment delay, h	3.7 (3)	3.6 (3)	4.1 (3)	.05
Transported	390 (47%)	317 (48%)	73 (40%)	.04
Culprit vessel				
LMCA	12 (1%)	10 (2%)	2 (1%)	1
AD	371 (42%)	284 (43%)	87 (48%)	.31
CxA	101 (12%)	85 (13%)	16 (9%)	.13
RCA	351 (44%)	273 (42%)	78 (43%)	.87
Number of diseased vessels	1.5 (0.8)	1.47 (0.8)	1.58 (0.8)	.09
Multiple vessel disease	273 (33%)	204 (31%)	69 (38%)	.11
Single vessel disease	565 (67%)	451 (68%)	114 (62%)	.11
Two vessels	130 (16%)	99 (15%)	31 (17%)	.56
Three vessels	143 (17%)	105 (16%)	38 (21%)	.15
Glycoprotein IIb/IIIa inhibitors	463 (55%)	360 (55%)	103 (56%)	.80
Stent	789 (94%)	618 (94%)	171 (93%)	.21
Successful procedure	775 (93%)	611 (93%)	164 (90%)	.11
Cardiogenic shock	118 (14%)	87 (12%)	41 (21%)	<.01
IABP	69 (8%)	50 (8%)	19 (10%)	.23
Electrical cardioversion	70 (8%)	61 (9%)	9 (5%)	.07
Temporary pacemaker	51 (6%)	34 (5%)	17 (9%)	.05
OTI	46 (6%)	34 (5%)	12 (7%)	.47

\*Data are shown as means (SD) or number of patients (%).

LMCA indicated left main coronary artery; AD, anterior descending artery; CxA, circumflex artery; RCA, right coronary artery; IABP, intraaortic balloon pump; OTI, orotracheal intubation.

The main predictors in women were cardiogenic shock, age, anterior infarction, and treatment delay, while in men they were cardiogenic shock, age, and multiple vessel disease.

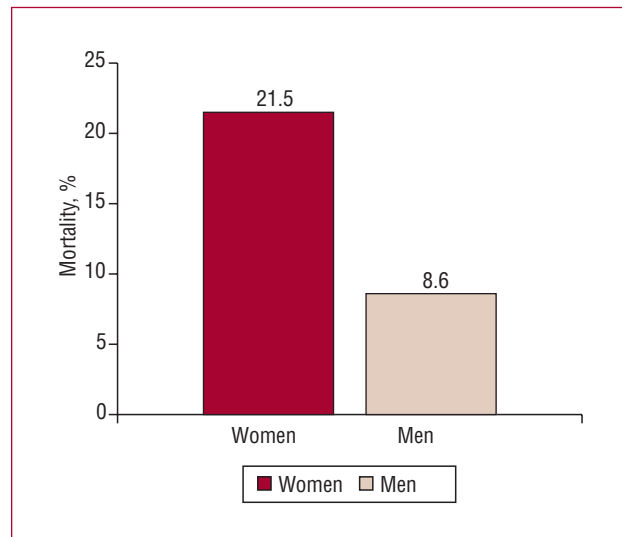
### Follow-Up After Hospital Discharge

Following hospital discharge, clinical follow-up was performed in 734 patients for a median of 35.4 months

**TABLE 3. Odds Ratio for Mortality in Women With ST-Segment Elevation Myocardial Infarction Treated by Primary Angioplasty\***

	OR (95% CI)	P
Unadjusted		
Women	2.9 (1.9-4.5)	<.01
Adjusted		
Women	2.5 (1.2-5.2)	.016

\*CI indicates confidence interval; OR, odds ratio adjusted for age, treatment delay, treatment success, diabetes mellitus, smoking, anterior myocardial infarction, number of vessels, and cardiogenic shock.

**Figure 2.** In-hospital mortality (%) according to sex in patients with ST-segment elevation acute myocardial infarction treated by primary angioplasty.

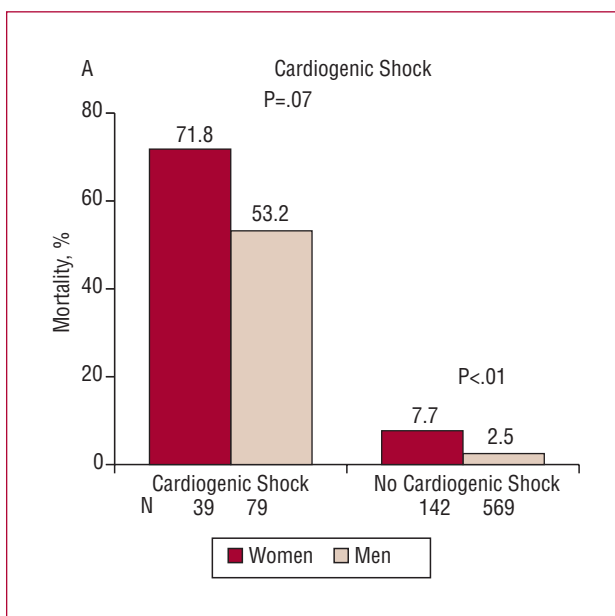
(interquartile range, 25.7 months). Follow-up was achieved in 98% of survivors. Of the 140 women included in follow-up, 18% died, compared with 9.3% of men. A

**TABLE 4. Univariate Predictors of In-Hospital Mortality\***

	Men		Women	
	OR (95% CI)	P	OR (95% CI)	P
Age	1.05 (1.02-1.07)	<.01	1.05 (1.01-1.1)	<.01
Smoking	0.58 (0.33-1.0)	.05	-	-
Previous CVS	4.5 (1.4-14.8)	.01	-	-
Number of diseased vessels	3.2 (2.3-4.5)	<.01	1.7 (1.1-2.6)	.13
Cardiogenic shock	46.8 (23-95)	<.01	31 (12.4-79.8)	<.01
Angiographic success	0.18 (0.1-0.4)	<.01	0.33 (0.1-0.9)	.03
Anterior AMI	1.6 (0.9-2.8)	.1	1.8 (0.9-3.6)	.13
Time to treatment	1.1 (1.0-1.2)	<.01	1.1 (1-1.3)	.05
VF	2.7 (1.3-5.6)	<.01	1.9 (0.5-7.9)	.39
AVB	8.2 (3.9-17.5)	<.01	17 (5.2-57.1)	<.01
OTI	23 (11-49)	<.01	6 (1.8-20)	<.01

\*CVS indicates cardiovascular surgery; AMI, acute myocardial infarction; VF, ventricular fibrillation; AVB, atrioventricular block requiring pacing; ; OTI, orotracheal intubation; CI, confidence interval; OR, odds ratio.

Estimators for previous cardiovascular surgery or smoking in women could not be calculated due to an insufficient number of cases.



**Figure 3.** In-hospital mortality according to sex in different subsets of patients. A) Presence or absence of cardiogenic shock. B) Age above or below 75 years. C) Stratification according to cardiogenic shock and age above or below 75 years.

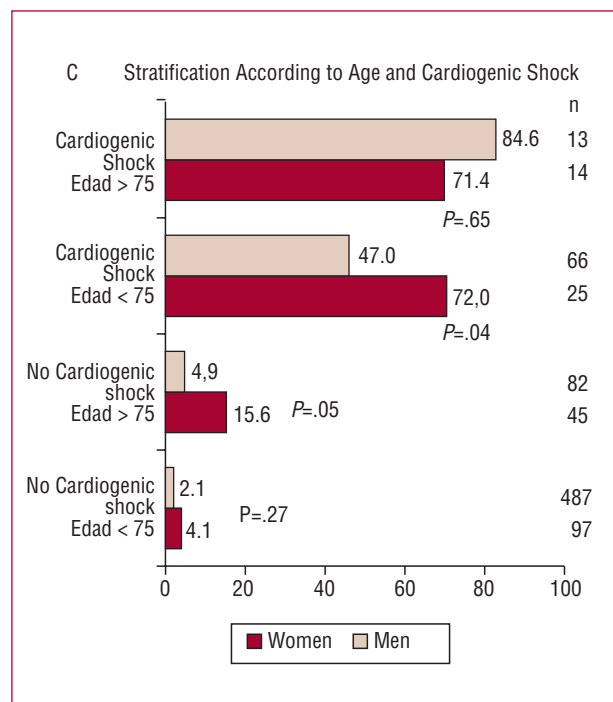
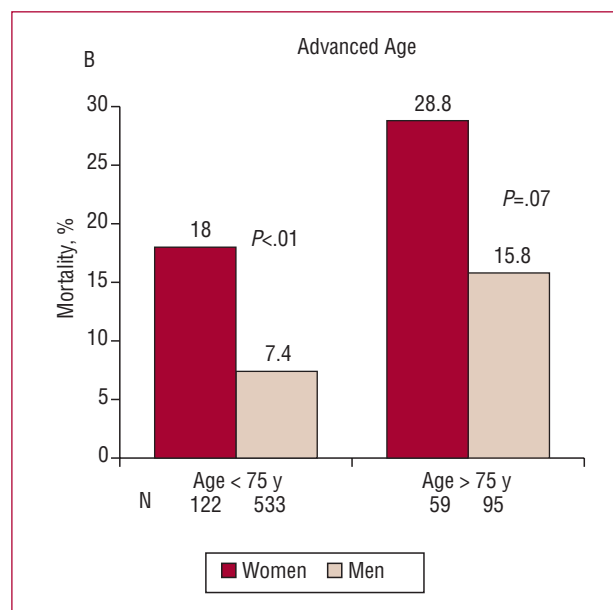
worse survival curve after hospital discharge was obtained for women in the univariate analysis (log-rank test=7.08,  $P<.01$ ; Figure 5), but that difference was not statistically significant following adjustment for age (Figure 6). No differences were observed according to sex for repeat admission, admission due to cardiac causes, or the requirement for repeat revascularization during follow-up (Table 6).

## DISCUSSION

Despite treatment of STEMI with primary angioplasty, in-hospital mortality continues to be high in Spain when compared with that of men following adjustment for baseline clinical characteristics.

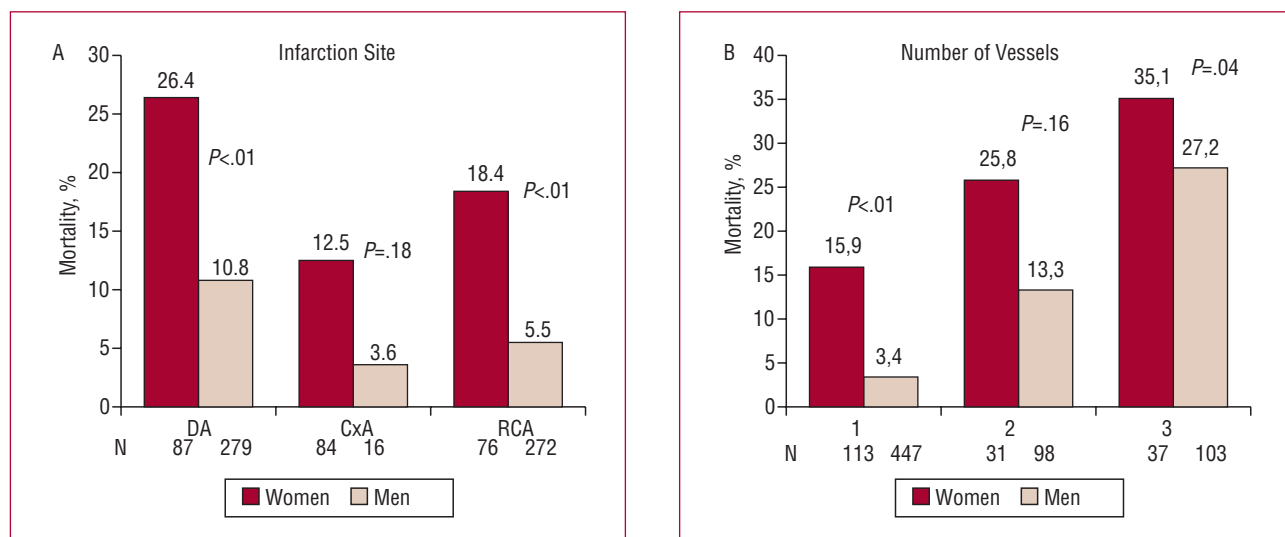
In survivors following hospital discharge the influence of sex on mortality is diluted in long-term follow-up when we adjust for age. During follow-up after hospital discharge we also do not observe significant differences between men and women in terms of readmission for cardiovascular causes or repeat revascularization.

Ischemic heart disease is the main cause of death in women of all ages in the Western world.<sup>1</sup> Previous studies have shown lower short-term survival in women with acute myocardial infarction,<sup>11-13</sup> but there is a lack of consensus on whether sex is independent of other indicators of poor prognosis such as age, treatment delay, less aggressive treatment, and greater intracranial hemorrhage following thrombolysis,<sup>4</sup> and few studies have assessed these differences following mechanical reperfusion.<sup>6,7,9</sup>



Unlike in previous reports, in this study we analyzed the results, both in-hospital and during long-term clinical follow-up, of a population of women from southeast Spain who, irrespective of age, received appropriate mechanical reperfusion treatment, including stent implantation and administration of glycoprotein IIb/IIIa inhibitors in a large percentage of cases. The data from our study correspond to consecutive patients from day-to-day clinical practice, thereby eliminating the inclusion bias that often affects women.<sup>14</sup>

As in other studies,<sup>7,9</sup> the women included in this study were older and presented a worse cardiovascular profile

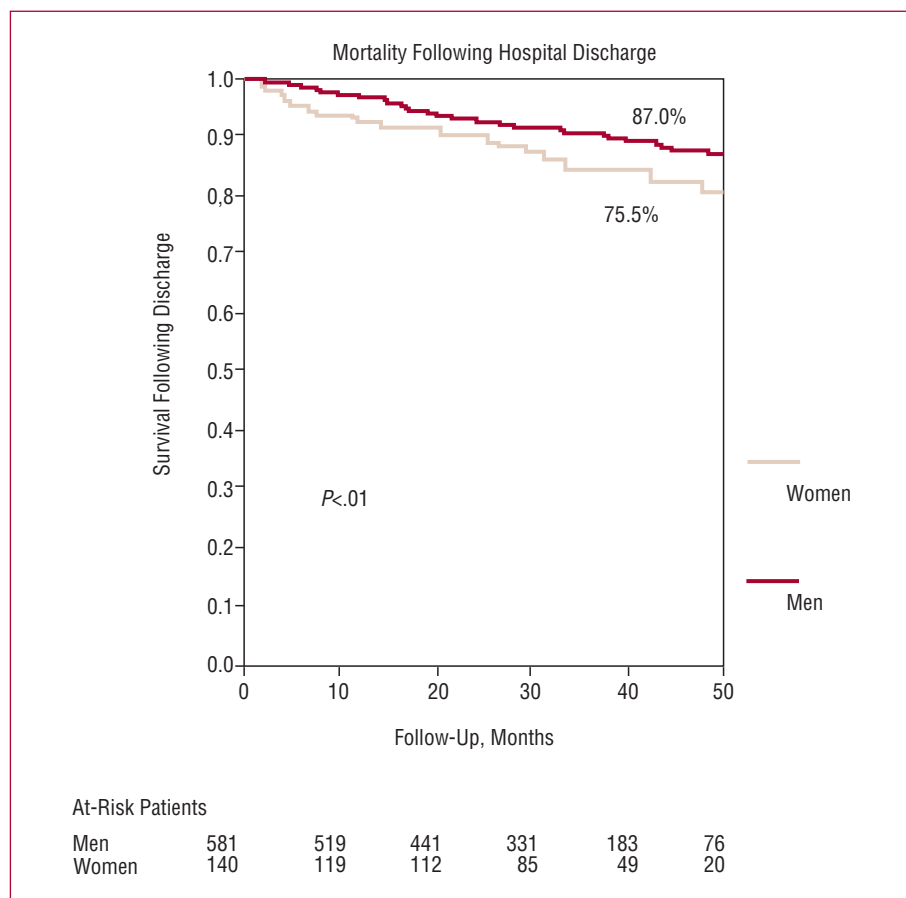


**Figure 4.** In-hospital mortality according to sex in different subsets of patients. A) Culprit artery. B) Number of diseased vessels. RCA indicates right coronary artery; CxA, circumflex artery; DA, descending artery.

than the men. This accumulation of cardiovascular risk factors is common in postmenopausal women. This factor may be associated with metabolic differences that are exacerbated by imbalances in endogenous and exogenous sex hormones,<sup>15</sup> which influence body fat distribution,

insulin resistance, lipid metabolism, clotting factors, and inflammation.<sup>16</sup>

The percentage of women with STEMI in our study population was significantly lower than that of men, an observation that is consistent with the results of previous



**Figure 5.** Kaplan-Meier curve for survival following hospital discharge.

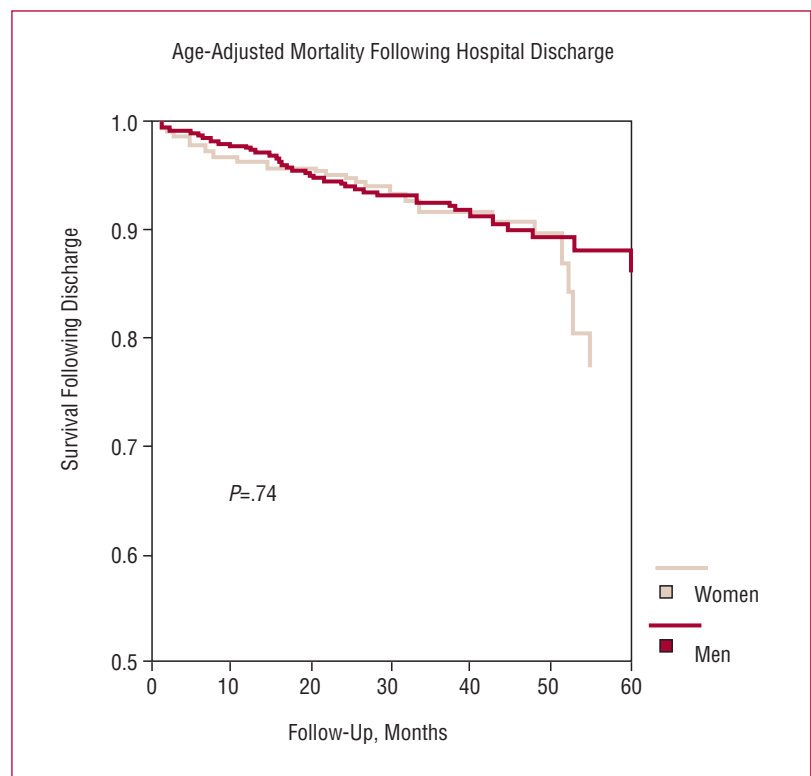
**TABLE 5. Predictors in the Multivariate Analysis of In-Hospital Mortality According to Sex in ST-Segment Elevation Myocardial Infarction Treated by Primary Angioplasty\***

Men†			Women‡		
Predictors	OR (95% CI)	P	Predictors	OR (95% CI)	P
Age	1.2 (1-1.4)	.03	Age	1.3 (1-1.7)	.03
Cardiogenic shock	38.8 (18-83)	<.01	Time to treatment	1.2 (1-1.4)	.06
Multiple vessel disease		<.01	Cardiogenic shock	36.8 (12.7-107)	<.01
2 vessels	2.9 (1.1-7.6)	.03	Caused by AD	2.6 (0.9-7.1)	.06
3 vessels	6.2 (2.6-14.8)	<.01			

\*AD indicates anterior descending artery; CI, confidence interval; OR, odds ratio (age introduced in quintiles).

†In analysis of multiple vessel disease, single vessel disease was taken as the reference category.

‡Homer and Lemeshow test:  $\chi^2=2.548$ ;  $P=.652$ ; specificity, 97.4%; sensitivity, 52.7%.  $\chi^2=5.866$ ;  $P=.662$ ; specificity, 93.6%; sensitivity, 67.6%.



**Figure 6.** Effect of sex on survival following hospital discharge after ST-segment elevation myocardial infarction treated by primary angioplasty. Cox analysis with adjustment for age.

studies. This may be related to the greater incidence of ischemic heart disease presenting as STEMI in men compared with more common manifestation in the form of angina symptoms in women.<sup>17-19</sup>

Previous studies in patients with STEMI have found larger differences in mortality according to sex in younger patients, while mortality tends to equalize in older patients, suggesting an interaction between age and sex that has not always been significant.<sup>13,20,21</sup> The women in our study population were of an advanced age (mean, 70 years), almost a decade older than the men. In-hospital mortality was significantly higher in older women compared with older men, and a marked tendency was seen towards increased mortality in women under 75 years compared with men in the same age group. No significant interaction

**TABLE 6. Events According to Sex Following Hospital Discharge After ST-Segment Elevation Myocardial Infarction Treated by Coronary Angioplasty\***

	Events		
	Men	Women	RR (95% CI)
Death	54 (9.3%)	25 (18.0%)	1.9 (1.2-3)
Following adjustment for age			1.15 (0.7-1.9)
Admissions	256 (43.2%)	71 (50.0%)	0.92 (0.7-1.2)
Admissions for cardiovascular causes	159 (26.9%)	34 (23.9%)	0.96 (0.7-1.4)
Repeat revascularization	117 (19.8%)	25 (17.6%)	1.2 (0.8-1.8)

\*Data are shown as number of patients (%) and relative risk for the event compared with men.

CI indicates confidence interval; RR, relative risk.

was observed between age and sex, indicating greater in-hospital mortality in women independently of age group. This difference from previous studies may be justified by the baseline clinical characteristics of the populations, the size of the sample, and the mechanical reperfusion therapy used in our population.<sup>22</sup>

Consistent with previous studies,<sup>13,23,24</sup> the women presented a greater time with symptoms of STEMI when they arrived in the catheterization laboratory and greater hemodynamic instability during the procedure. Likewise, the length of time from onset of the infarction was the only modifiable factor among the predictors of worse prognosis, both in men and women. Female sex is an independent risk factor for the development of cardiogenic shock as a complication of acute myocardial infarction.<sup>25</sup> The increased mortality in women with acute myocardial infarction and cardiogenic shock may be related to the increased frequency of mitral regurgitation, septal rupture, free wall rupture, ventricular aneurysm, asystole, and advanced block.<sup>26</sup> The crude differences in in-hospital mortality between women and men are maintained in patients with or without cardiogenic shock. The between-sex differences were only nonsignificant in young patients without cardiogenic shock (4.1% vs 2.1%,  $P=.27$ ), possibly due to the size of the sample.

Likewise, the differences in in-hospital mortality between the sexes remained significant in other subsets of patients, such as those who presented single-vessel disease or in inferior infarctions, a finding that is consistent with the results of previous studies.<sup>21</sup>

Consistent with the findings of other studies, malignant ventricular arrhythmias<sup>26</sup> were less common in women than men, and women more commonly presented advanced atrioventricular block and asystole.<sup>11</sup> Those findings may be explained by the occurrence in women of greater vagal activation, which could protect against arrhythmia as a result of complete coronary artery occlusion.<sup>27-29</sup>

It has been reported previously that the use of diagnostic and therapeutic procedures is low in women with STEMI.<sup>30-34</sup> Previous studies also show that following acute myocardial infarction, coronary angiography is employed less often in women than men, and that this is associated with an increase in short-term mortality, especially in older people.<sup>35</sup> In the present study, all patients were treated by mechanical reperfusion in the first few hours of infarction, the success of the procedure was similar in both groups, and unlike in previous studies,<sup>7</sup> a large percentage of patients received stents and glycoprotein IIb/IIIa inhibitors.

In survivors following hospital discharge, despite women presenting a higher crude mortality, no differences were observed when the results were adjusted for age. Previous studies have reported similar results in terms of mortality following hospital discharge.<sup>36,37</sup> In our study, there were also no differences in terms of readmission

for cardiovascular causes or repeat revascularization. The high rate of readmission for any cause may be linked to the advanced age of the population, which is associated with high comorbidity.

It has been suggested that pathophysiologic differences contribute to the increased mortality seen in women with STEMI. Estrogens, which protect against coronary atherosclerosis,<sup>38</sup> could make vulnerable plaques less stenotic.<sup>39,40</sup> Less severe rupture and occlusive thrombosis of those plaques could hinder the development of myocardial preconditioning and collateral circulation, thereby worsening the prognosis of infarction. Between-sex differences in acute coronary syndrome may be associated with variation in thrombolytic and fibrinolytic activity.<sup>41</sup> The higher percentage of women with heart failure in the presentation of infarction may also reflect greater diastolic dysfunction in women.<sup>42</sup> Other hypotheses regarding the pathophysiologic mechanisms underlying increased mortality in myocardial infarction, especially in young women, include the presence of abnormalities in the estrogen receptor, ovary dysfunction,<sup>43</sup> premature menopause, and proinflammatory states.<sup>44</sup>

## Limitations

In the referral hospital for primary angioplasty, patients with STEMI were systematically treated by mechanical reperfusion. In other hospitals, however, a significantly lower proportion of women were referred for primary angioplasty, suggesting a possible selection bias relating to sex in the use of the procedure. A higher crude mortality outside hospital has been described previously in women,<sup>45,46</sup> and that may bias the percentage of women who receive hospital treatment. Ventricular function was not included in the predictors of long-term mortality. Despite worse in-hospital prognosis, previous studies have not found more extensive necrosis or worse ventricular function in women.<sup>4,6,7,47,48</sup> The use of concomitant medication such as beta blockers, angiotensin converting enzyme inhibitors, or statins during hospital admission or following discharge was not recorded, meaning that the possibility of differences in the administration of such drugs according to sex cannot be ruled out.

When considered alongside the published literature, our results contribute to describing currently existing differences between the sexes in patients with ischemic heart disease and the need to improve, especially in women, areas such as diagnosis and early complete treatment, the development of lines of research into pathophysiologic characteristics of ischemic heart disease in women, and the formation of working parties dedicated to women. These concerns have led to the publication of specific guidelines on the prevention and percutaneous treatment of cardiovascular disease in women.<sup>14</sup>

## CONCLUSIONS

Despite new advances in the treatment of STEMI, in-hospital mortality in women is twice that of men. This result is only partially explained by more advanced age and other baseline characteristics of that group. In long-term follow-up of survivors after hospital discharge, no significant differences in mortality were observed after adjustment for age.

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