Med Intensiva. 2017;41(2):70–77

medicina intensiva

www.elsevier.es/medintensiva

ORIGINAL

Gender gap in medical care in ST segment elevation myocardial infarction networks: Findings from the Catalan network Codi Infart☆

D. Fernández-Rodríguez[a,b], A. Regueiro[a], J. Cevallos[a], X. Bosch[a], X. Freixa[a], M. Trilla[a], S. Brugaletta[a], V. Martín-Yuste[a], M. Sabaté[a], F. Bosa-Ojeda[c], M. Masotti[a,*], on behalf of the Investigators of the Codi Infart Registry

[a] *Department of Cardiology, Clínic Hospital, University of Barcelona, Barcelona, Spain*
[b] *Department of Cardiology, Nuestra Señora de Candelaria University Hospital, University of La Laguna, San Cristóbal de La Laguna, Santa Cruz de Tenerife, Spain*
[c] *Department of Cardiology, Canarias University Hospital, University of La Laguna, San Cristóbal de La Laguna, Santa Cruz de Tenerife, Spain*

Received 31 March 2016; accepted 16 June 2016
Available online 6 March 2017

KEYWORDS
Gender;
Acute ST-elevation myocardial infarction;
Primary percutaneous coronary intervention;
Network

Abstract
Objective: To assess the impact of gender upon the prognosis and medical care in a regional acute ST-elevation myocardial infarction management network.
Design: An observational study was made of consecutive patients entered in a prospective database.
Scope: The Catalan acute ST-elevation myocardial infarction management network.
Patients: Patients treated between January 2010 and December 2011.
Interventions: Primary angioplasty, thrombolysis or conservative management.
Variables of interest: Time intervals, proportion and type of reperfusion, overall mortality, and in-hospital complication and overall mortality at 30 days and one year were compared in relation to gender.
Results: Of the 5831 patients attended by the myocardial infarction network, 4380 had a diagnosis of acute ST-elevation myocardial infarction, and 961 (21.9%) were women. Women were older (69.8 ± 13.4 vs. 60.6 ± 12.8 years; $p < .001$), had a higher prevalence of diabetes (27.1 vs. 18.1%, $p < .001$), Killip class > I (24.9 vs. 17.3%; $p < .001$) and no reperfusion (8.8 vs. 5.2%; $p < .001$) versus men. In addition, women had greater delays in medical care (first medical contact-to-balloon: 132 vs. 122 min; $p < .001$, and symptoms onset-to-balloon: 236 vs. 210 min; $p < .001$). Women

☆ Please cite this article as: Fernández-Rodríguez D, Regueiro A, Cevallos J, Bosch X, Freixa X, Trilla M, et al. Brecha de género en los cuidados médicos en las redes de atención al infarto agudo de miocardio con elevación del segmento ST: hallazgos de la red catalana Codi Infart. Med Intensiva. 2017;41:70–77.

* Corresponding author.
E-mail address: masotti@clinic.ub.es (M. Masotti).

presented higher percentages of overall in-hospital complications (20.6 vs. 17.4%; $p = .031$), in-hospital mortality (4.8 vs. 2.6%; $p = .001$), 30-day mortality (9.1 vs. 4.5%; $p < .001$) and one-year mortality (14.0 vs. 8.3%; $p < .001$) versus men. Nevertheless, after multivariate adjustment, no gender differences in 30-day and one-year mortality were observed.
Conclusions: Despite a higher risk profile and poorer medical management, women present similar 30-day and one-year outcomes as their male counterparts in the context of the myocardial infarction management network.

PALABRAS CLAVE
Género;
Infarto agudo de miocardio con elevación del segmento ST;
Angioplastia primaria;
Red

Brecha de género en los cuidados médicos en las redes de atención al infarto agudo de miocardio con elevación del segmento ST: hallazgos de la red catalana Codi Infart

Resumen
Objetivo: Evaluar el impacto del género sobre el pronóstico y el manejo en una red regional de atención al infarto agudo de miocardio con elevación del segmento ST.
Diseño: Estudio observacional sobre una base de pacientes consecutivos recogida prospectivamente.
Ámbito: Red catalana de atención al infarto agudo de miocardio con elevación del segmento ST.
Pacientes: Pacientes atendidos entre enero de 2010 y diciembre de 2011.
Intervenciones: Angioplastia primaria, fibrinólisis o manejo conservador.
Variables de interés: Se compararon, según el género, intervalos de tiempo, proporción y tipo de reperfusión, mortalidad global y complicaciones intrahospitalarias y mortalidad global a 30 días y un año.
Resultados: De 5.831 pacientes atendidos, 4.380 tenían diagnóstico de infarto agudo de miocardio con elevación del segmento ST, siendo 961 (21,9%) de ellos mujeres. Estas tenían mayor edad (69,8 ± 13,4 frente a 60,6 ± 12,8 años, p < 0,001), mayor prevalencia de diabetes (27,1 frente a 18,1%, p < 0,001), Killip > I (24,9 frente a 17,3%, p < 0,001) y ausencia de reperfusión (8,8 frente a 5,2%, p < 0,001) que los hombres. Además, las mujeres presentaban mayores retrasos en la atención (primer contacto médico-balón: 132 frente a 122 min, p < 0,001; inicio de síntomas-balón: 236 frente a 210 min, p < 0,001), más complicaciones intrahospitalarias (20,6 frente a 17,4%, p = 0,031) y mortalidad intrahospitalaria, a 30 días y un año (4,8 frente a 2,6%, p = 0,001; 9,1 frente a 4,5%, p < 0,001; 14,0 frente a 8,3%, p < 0,001). Sin embargo, tras el análisis multivariado no hubo diferencias en mortalidad a 30 días y un año.
Conclusiones: A pesar del peor perfil de riesgo y el peor tratamiento recibido, las mujeres presentaron similares resultados a 30 días y un año que sus homólogos masculinos atendidos por una red de atención al infarto.

Introduction

ST-segment elevation acute myocardial infarction (STEMI) is one of the greatest public health problems in society today.[1,2] Traditionally, women with STEMI have been considered to have a poorer prognosis than men with the same disorder,[3] probably because they receive less optimum management (fewer hospital admissions, a lesser percentage of medical treatments recommended by the clinical practice guides, and a lesser percentage of primary angioplasty [PA]),[4] with a greater delay in applying reperfusion therapies.[5] However, recent studies, after adjusting for confounding factors, have identified no gender-related differences in terms of the treatment and prognosis of the disease.[6,7]

The benefits derived from reperfusion therapy in STEMI are conditioned to time.[8] Primary angioplasty, performed within the recommended time window, can reduce the mortality and reinfarction risk compared with fibrinolysis.[9] Likewise, moving STEMI patients from hospitals where PA is not available 24 h a day, 7 days a week (24/7), to centers with PA 24/7 has been shown to be a feasible and safe strategy.[10] For this reason, PA is regarded as the treatment of choice in STEMI, provided it is performed by an experienced operator within 120 min after first medical contact (FMC).[1]

The implantation of STEMI management networks has contributed to expand reperfusion therapy, fundamentally involving PA, and thus has helped to generalize optimum treatment for each patient according to the time window

recommended by the clinical practice guides.[11] However, only limited information is available on the impact of patient gender in STEMI cases attended by networks specifically designed to the effect.[4,12] The present study was designed to analyze the impact of gender in terms of the medical care received and upon patient mortality (in-hospital, after 30 days and at one year) in a population attended by a regional STEMI management network.

Material and methods

Study population, STEMI management network and the *Codi Infart* registry

The present multicentric observational study is fundamented upon a prospective database of consecutive STEMI patients attended by the Catalan STEMI management network (the *Codi Infart* registry) from January 2010 to December 2011.

The Autonomous Community of Catalonia is located in North-Eastern Spain and has a population of approximately 7.5 million inhabitants. A STEMI management network was implanted in Catalonia in June 2009.[13,14] The network divided Catalonia into reference areas for the 10 pre-existing hospitals with the capacity to perform PA, with the aim of affording the reperfusion therapy best suited to each individual patient. The *Codi Infart* comprised 5 basic elements: (1) The ambulances of the Medical Emergencies Service (*Servei d'Emergencies Mèdiques* [SEM]), staffed by physician/s or nurse/s capable of diagnosing the symptoms, interpreting the electrocardiogram (ECG) tracings and of administering fibrinolytic therapy; (2) The SEM coordination center which decided the reperfusion strategy and coordinated the logistics among ambulances, district hospitals and hospitals with the capacity to perform PA; (3) The 10 hospitals with the capacity to perform PA (5 of which had 24/7 availability); (4) The Intensive Care Units (ICUs) or Coronary Units of all the hospitals participating in the project, and which received the patients after undergoing reperfusion treatment; and (5) The inclusion of all the patients attended by the network in a mandatory prospective registry (the Codi Infart registry).

Briefly, the protocol specified that when a medical professional diagnosed STEMI on the basis of clinical criteria and the ECG tracing in the context of FMC, the network was to be activated and the strategy would be chosen according to the clinical practice guides.[1] All patients with STEMI directly admitted to a center with the capacity to perform PA underwent PA, while those patients initially attended in hospitals without PA, in primary care centers or directly by the SEM were moved to centers where PA was available, according to the risk profile involved and if the time to PA was expected to be less than 120 min. If the time to PA was expected to be longer than 120 min, fibrinolytic therapy was provided if compatible with the clinical condition of the patient, and only in the case of failed fibrinolysis was the patient transferred for rescue angioplasty. Secondary prevention in turn was prescribed according to common medical practice in each center.[1,2,14]

The *Codi Infart* registry is implemented according to the principles of the Declaration of Helsinki, and complies with all the legal requirements. All the centers were encouraged to keep the registry, and all the patients attended by the network were required to be included in it. Demographic and clinical data were collected, together with information on the procedure, the time intervals, and the in-hospital complications, with telephone follow-up after 30 days. Mortality due to all causes after one year was documented by crossing the data of each patient with the database of the Spanish National Statistics Institute (*Instituto Nacional de Estadística* [INE]) (death certificates).

Study variables

In line with the purpose of the study, all the variables were analyzed according to gender. The primary endpoint was mortality due to all causes as determined after one year. The secondary clinical endpoints included: mortality due to all causes in-hospital and after 30 days, and in-hospital complications, defined as the combination of ventricular fibrillation, ventricular tachycardia, asystolia, complete atrioventricular block, atrial fibrillation, cardiogenic shock or the need for mechanical ventilation, and each of the individual components considered separately. Cardiogenic shock was defined as the need for intravenous inotropic drugs and/or intra-aortic balloon counterpulsation in order to keep the systolic blood pressure (SBP) >90 mmHg.[1] Other secondary endpoints related to medical treatment were also evaluated, such as the type of reperfusion therapy provided, and the following management intervals: symptoms onset-FMC, FMC-diagnostic ECG, diagnostic ECG-balloon, FMC-balloon, and symptoms onset-balloon (total ischemia time).[15] First medical contact in turn was defined as the first contact with the healthcare system, where the patient was attended by a physician or nurse on an in-hospital or pre-hospital basis, and with the capacity to activate the STEMI management network.[15]

All the events were assigned by the Catalan Health Department (*Servei Català de la Salut: CatSalut; Departament de Salut, Generalitat de Catalunya*). As commented above, all study variables were analyzed according to gender.

Statistical analysis

The normal distribution of continuous variables was assessed based on the Kolmogorov–Smirnov test. Those variables found to present a normal distribution were expressed as the mean (standard deviation [SD]), while those lacking a normal distribution were expressed as the mean (interquartile range [IQR])–comparisons being made using the Student's *t*-test or Mann–Whitney *U* test as applicable. Categorical variables in turn were expressed as number (percentage) and were compared using the chi-squared test.

Cox proportional hazards regression models were developed to evaluate the association between gender (exposure variable) and overall mortality after 30 days and one year. We performed an exploratory univariate analysis, and the covariables with clinical justification or $p < 0.10$ were entered in the Cox regression models. The following variables were included in the models: gender, age, diabetes mellitus, previous myocardial infarction, previous

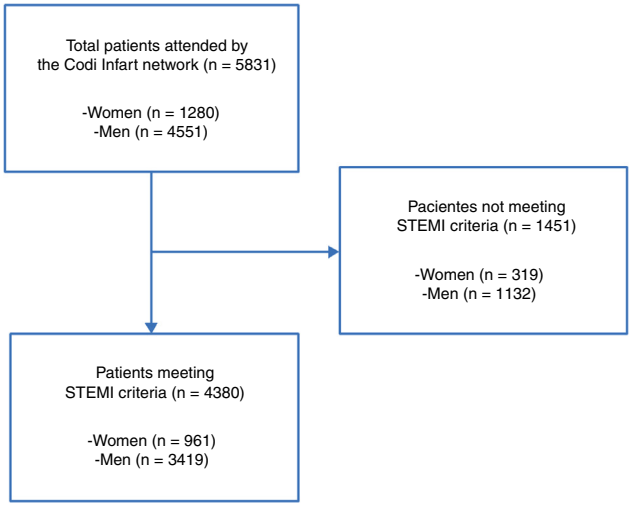

Figure 1 Study flow chart. STEMI: ST-segment elevation acute myocardial infarction.

angioplasty, previous coronary bypass surgery, diagnostic ECG, location of myocardial infarction, Killip class upon admission, place of FMC, time intervals, and treatment received.

The results were reported as hazard ratios (HR) with the corresponding 95% confidence interval (95%CI). All *p*-values were two-tailed, and statistical significance was considered for $p < 0.05$. The SPSS® version 20.0 statistical package (SPSS Inc., Chicago, IL, USA) was used throughout.

Results

A total of 5831 patients with suspected STEMI were activated within the *Codi Infart* network between January 2010 and December 2011. The final analysis involved 4380 patients (75.1%). The flow chart is shown in Fig. 1.

Clinical characteristics and reperfusion strategies

Of the 4380 patients analyzed, 961 (21.9%) were females and 3419 (78.1%) were males. The baseline characteristics of both groups are shown in Table 1. The women were comparatively older (69.8 ± 13.4 vs. 60.6 ± 12.8 years, respectively; $p < 0.001$), with a greater prevalence of diabetes mellitus (27.1 vs. 18.1%; $p < 0.001$) and a greater prevalence of Killip class >I upon admission (24.9 vs. 17.3%; $p < 0.001$). Furthermore, the female group showed a lesser prevalence of previous myocardial infarction (6.9 vs. 9.7%; $p = 0.007$), previous angioplasty (3.9 vs. 6.9%; $p < 0.001$) and previous coronary bypass procedures (0.3 vs. 1.1%; $p = 0.022$) compared with the male group. The place of FMC also differed significantly between the two groups. In turn, it should be mentioned that the female group comprised a greater percentage of non-reperfused patients compared with the male group (8.8 vs. 5.2%; $p < 0.001$).

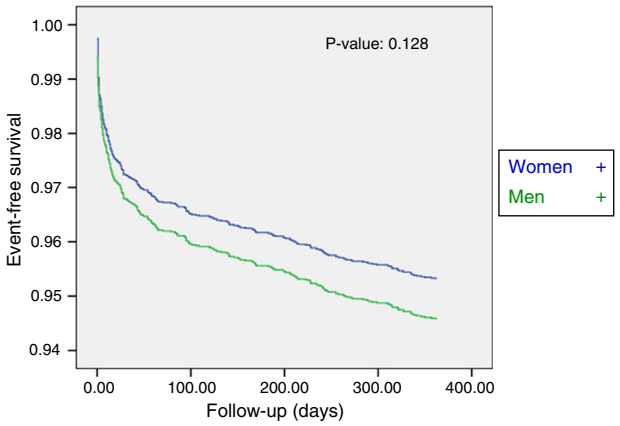

Figure 2 Cox regression curve corresponding to one-year mortality due to all causes.

Time intervals

In comparison with the male population, the women that underwent PA showed greater delays in the following management time intervals: symptoms onset-FMC (90 vs. 74 min; $p < 0.001$), FMC-diagnostic ECG (26 vs. 22 min; $p < 0.003$), diagnostic ECG-balloon (83 vs. 80 min, $p = 0.020$), FMC-balloon (132 vs. 122 min; $p < 0.001$) and symptoms onset-balloon (total ischemia time) (236 vs. 210 min; $p < 0.001$).

The comparative data referred to the mentioned time intervals are shown in Table 2.

Clinical events

The data comparing the clinical events between the groups are shown in Table 3. Overall, women presented a greater percentage of in-hospital complications (22.2 vs. 19.0%; $p = 0.031$). In particular, the female group showed a greater presence of atrioventricular block (6.1 vs. 3.7%; $p = 0.001$), atrial fibrillation (3.4 vs. 2.2%; $p = 0.032$) and cardiogenic shock (9.7 vs. 7.9%; $p < 0.001$) than the male group. Furthermore, women had a greater overall in-hospital mortality rate (4.8 vs. 2.6%; $p = 0.001$), overall 30-day mortality rate (9.1 vs. 4.5%; $p < 0.001$) and overall one-year mortality rate (14.0 vs. 8.3%; $p < 0.001$).

However, following multivariate adjustment of the data, no gender differences were observed in the overall 30-day mortality rate (hazard ratio [HR] adjusted to 30 days [95%CI]: 1.25 [0.94–1.65]; $p = 0.123$; HR adjusted to one year [95%CI]: 0.88 [0.69–1.07]; $p = 0.128$). The Cox regression curve for mortality due to all causes after one year is shown in Fig. 2.

Discussion

The main conclusions of our study were: (1) women with STEMI had a comparatively worse risk profile and a greater proportion of in-hospital complications and overall mortality; (2) women received less reperfusion treatment and suffered longer delays in medical assistance compared with men; and (3) after adjusting for confounding factors, women

Table 1 Patient baseline clinical characteristics and management.

Characteristics	Women (n = 961)	Men (n = 3419)	*p*-Value
Population, n (%)	961 (21.9)	3419 (78.1)	**<0.001**
Age (years), mean (SD)	69.8 (13.4)	60.6 (12.8)	**<0.001**
Diabetes mellitus, n (%)	260 (27.1)	620 (18.1)	**<0.001**
Previous MI, n (%)	66 (6.9)	331 (9.7)	**0.007**
Previous angioplasty, n (%)	37 (3.9)	236 (6.9)	**<0.001**
Previous CB, n (%)	3 (0.3)	39 (1.1)	**0.022**
Diagnostic ECG, n (%)			0.578
ST-segment elevation	883 (99.1)	3179 (99.3)	
Left bundle block	9 (0.9)	24 (0.7)	
Location, n (%)			
Anterior	435 (45.3)	1487 (43.5)	0.339
Inferior	460 (47.9)	1738 (50.8)	0.108
Lateral	105 (10.9)	360 (10.5)	0.809
Killip class upon admission, n (%)			**<0.001**
I	722 (75.1)	2826 (82.7)	
II	100 (10.4)	261 (7.6)	
III	46 (4.8)	63 (1.8)	
IV	93 (9.7)	269 (7.9)	
Killip >I upon admission, n (%)	239 (24.9)	593 (17.3)	**<0.001**
Place of FMC, n (%)			**0.042**
Hospital without PA	383 (39.9)	1266 (37.0)	
Hospital with PA	156 (16.2)	483 (14.1)	
Primary care center	160 (16.7)	666 (19.5)	
SEM	262 (27.3)	1004 (29.4)	
Treatment, n (%)			
Fibrinolysis	68 (7.1)	285 (8.3)	0.227
PA	808 (84.1)	2956 (86.5)	0.066
No reperfusion therapy	85 (8.8)	178 (5.2)	**<0.001**

PA: primary angioplasty; SD: standard deviation; ECG: electrocardiogram; CB: coronary bypass; MI: myocardial infarction; FMC: first medical contact.
The highlighted data are statistically significant.

Table 2 Medical management intervals in patients subjected to primary angioplasty.

Medical management intervals (min), mean [IQR]	Women (n = 808)	Men (n = 2956)	*p*-Value
Population, n (%)	808 (21.5)	2956 (78.5)	**<0.001**
Symptoms onset-FMC	90 [42–180]	74 [35–162]	**<0.001**
FMC-diagnostic ECG	26 [12–51]	22 [12–45]	**0.003**
Diagnostic ECG-balloon	83 [62–115]	80 [60–110]	**0.020**
FMC-balloon	132 [99–183]	122 [92–170]	**<0.001**
Symptoms onset-balloon (total ischemia time)	236 [169–360]	210 [150–315]	**<0.001**

ECG: electrocardiogram; FMC: first medical contact; IQR: interquartile range.
The highlighted data are statistically significant.

and men showed similar rates referred to mortality due to all causes after both 30 days and one year of follow-up.

STEMI management network and gender gap in medical care

The implementation of strategies designed to facilitate STEMI patient access to the medical care system has been shown to reduce delays in percutaneous coronary intervention,[16,17] lessen the mortality rate,[18] and lower the global hospital costs.[19]

Despite the improvements in medical care resulting from introduction of the STEMI management networks, the gender gap in patient management is seen to persist. Indeed, in our study women suffered greater delays and underwent a lesser proportion of revascularization procedures than men. Previous studies have shown that women suffer greater delays in medical assistance, as evidenced by longer door-balloon times and longer total ischemia times.[20–23] By allowing ECG recordings in the home, out-hospital activation of hemodynamic systems and direct patient transfer to the Hemodynamics Unit via the SEM, the STEMI

Table 3 Clinical events.

	Women (n = 961)	Men (n = 3419)	*p*-Value
Population, n *(%)*	961 (21.9)	3419 (78.1)	**<0.001**
In-hospital complications	198 (20.6)	594 (17.4)	**0.031**
Ventricular fibrillation	26 (2.7)	106 (3.1)	0.594
Ventricular tachycardia	27 (2.8)	81 (2.4)	0.412
Asystolia	18 (1.9)	44 (1.3)	0.215
Complete atrioventricular block	59 (6.1)	126 (3.7)	**0.001**
Atrial fibrillation	33 (3.4)	74 (2.2)	**0.032**
Cardiogenic shock	93 (9.7)	269 (7.9)	**<0.001**
Mechanical ventilation	46 (4.8)	141 (4.1)	0.367
Overall mortality			
In-hospital mortality	46 (4.8)	89 (2.6)	**0.001**
Mortality after 30 days	87 (9.1)	154 (4.5)	**<0.001**
Mortality after one year	135 (14.0)	285 (8.3)	**<0.001**

The highlighted data are statistically significant.

management networks have been associated to lesser delays in medical care and lower mortality rates.[24,25]

Following implantation of the *Codi Infart* network, the female population still shows longer management intervals and lesser reperfusion rates than the male population. This gender gap in time intervals and reperfusion therapy could be explained by gender differences in the clinical presentation and physiopathology of STEMI. Such differences should be considered when evaluating and treating women with suspected of confirmed STEMI, since this is a population characterized by great diagnostic and therapeutic complexity.[26]

The comparatively older age and greater prevalence of diabetes mellitus among the women in our study is associated to a greater presence of atypical symptoms that can lead to patient delays in contacting the medical care system (patient delay), as well as to errors in the clinical assessment of STEMI which in turn result in delays once the patients have already entered the system (system delay).[1,20–23] These differences were evidenced by the fact that women showed greater delays in all the evaluated time intervals compared with the male group.

It also should be commented that although PA is currently the preferred reperfusion strategy in STEMI, particularly in women, because PA is able to reduce bleeding complications in females to a greater extent than in males,[9,27–29] the gender difference in reperfusion therapy persists in our network – as reflected by the greater percentage of women that did not receive therapy versus their male counterparts (8.8 vs. 5.2%; $p < 0.001$). The data obtained in our study are unable to offer an in-depth explanation for this difference, though it could be mediated in part by gender-related physiopathological variations in STEMI such as the greater incidence of spontaneous coronary dissection and coronary spasm in the female population.[1,26,27]

STEMI management network and outcome in women

The studies carried out in the thrombolysis era, such as the GUSTO IIB trial,[28] have shown women to experience a greater proportion of in-hospital complications and mortality after 30 days compared with men. The mentioned study also demonstrated an interaction between mortality and the female gender following the multivariate adjustment analysis.[28] These data were subsequently confirmed by other registries during the 1990s and opening years of the XXI century in Spain.[29,30]

The studies published following the generalized adoption of PA in routine clinical practice[6,7,27,31] also showed women to suffer greater in-hospital mortality than men. This could be explained by the differences in reperfusion rate and the worse risk profile of the women with STEMI in those studies.

Following their multivariate analysis, Lawesson et al.[32] found the one-year mortality rate to be 8% lower in women than in men. This was the first study in the context of STEMI to show women to suffer greater in-hospital mortality but lesser long-term mortality than men. Our study did not identify differences in the overall mortality rate after 30 days and one year between the two genders after adjusting for the confounding factors. The results obtained indicate that the implantation of STEMI management networks has contributed to equalize the middle- and long-term prognosis in males and females, and suggest that if both genders could receive reperfusion therapy and medical management intervals in the same way, the long-term prognosis could be even better in women than in men.

Study limitations

A first limitation of this study is the fact that it is a retrospective analysis of subgroups from a prospective database of the *Servei Català de la Salut* (*CatSalut*). Nevertheless, it is the largest Spanish study to date on the role of patient gender in patients attended by a specific STEMI management network. A second limitation is that the outcome after one year was only assessed on the basis of mortality due to all causes and other prognostic assessment parameters such as cardiac mortality, myocardial infarction or the need for further revascularization. A third limitation is the fact that a non-negligible percentage of patients did not receive reperfusion therapy and, as commented above, we do not have concrete data capable of explaining this

observation – since the collection of such information was not contemplated when the registry was designed. A fourth limitations is the fact that the data are referred to the Catalan population, representing a Mediterranean area, and therefore cannot be fully extrapolated to other geographical settings. Lastly, we do not have information on the extent of coronary disease (e.g., the number of diseased vessels) or on the drug treatment or interventional cardiological management provided in the course of patient follow-up, and which could also influence the extrapolation of our results.

Conclusions

The female population attended by our regional STEMI management network had a worse risk profile, received less reperfusion therapy and showed greater delays in medical management than the male population. However, following the multivariate adjustment analysis, the clinical outcomes after 30 days and one year in the female population were seen to be similar to those of their male counterparts.

Financial support

None.

Conflicts of interest

The authors declare that they have no conflicts of interest.

References

1. Steg PG, James SK, Atar D, Badano LP, Blömstrom-Lundqvist C, Borger MA, et al. ESC guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. Eur Heart J. 2012;33:2569–619.
2. Heras M, Marrugat J, Arós F, Bosch X, Enero J, Suárez MA, et al. Reduction in acute myocardial infarction mortality over a five-year period. Rev Esp Cardiol. 2006;59:200–8.
3. Vaccarino V, Krumholz HM, Berkman LF, Horwitz RI. Sex differences in mortality after myocardial infarction. Is there evidence for an increased risk for women? Circulation. 1995;91:1861–71.
4. Greenberg MR, Miller AC, Mackenzie RS, Richardson DM, Ahnert AM, Sclafani MJ, et al. Analysis of sex differences in preadmission management of ST-segment elevation (STEMI) myocardial infarction. Gend Med. 2012;9:329–34.
5. Milcent C, Dormont B, Durand-Zaleski I, Steg PG. Gender differences in hospital mortality and use of percutaneous coronary intervention in acute myocardial infarction: microsimulation analysis of the 1999 nationwide French hospitals database. Circulation. 2007;115:833–9.
6. Nauta ST, Deckers JW, van Domburg RT, Akkerhuis KM. Sex-related trends in mortality in hospitalized men and women after myocardial infarction between 1985 and 2008: equal benefit for women and men. Circulation. 2012;126:2184–9.
7. Berger JS, Elliott L, Gallup D, Roe M, Granger CB, Armstrong PW, et al. Sex differences in mortality following acute coronary syndromes. JAMA. 2009;302:874–82.
8. Lambert L, Brown K, Segal E, Brophy J, Rodes-Cabau J, Bogaty P. Association between timeliness of reperfusion therapy and clinical outcomes in ST-elevation myocardial infarction. JAMA. 2010;303:2148–55.
9. Keeley EC, Boura JA, Grines CL. Primary angioplasty versus intravenous thrombolytic therapy for acute myocardial infarction: a quantitative review of 23 randomised trials. Lancet. 2003;361:13–20.
10. Widimský P, Budesínský T, Vorác D, Groch L, Zelízko M, Aschermann M, et al. Long distance transport for primary angioplasty vs immediate thrombolysis in acute myocardial infarction. Final results of the randomized national multicentre trial – PRAGUE-2. Eur Heart J. 2003;24:94–104.
11. Regueiro A, Goicolea J, Fernández-Ortiz A, Macaya C, Sabaté M. STEMI Interventions: the European perspective and stent for life initiative. Intervent Cardiol Clin. 2012;1:6.
12. Hailer B, Naber C, Koslowski B, van Leeuwen P, Schäfer H, Budde T, et al. Gender-related differences in patients with ST-elevation myocardial infarction: results from the registry study of the ST elevation myocardial infarction network Essen. Clin Cardiol. 2011;34:294–301.
13. Regueiro A, Tresserras R, Goicolea J, Fernández-Ortiz A, Macaya C, Sabaté M. Primary percutaneous coronary intervention: models of intervention in Spain. EuroIntervention. 2012;8 Suppl. P:P90–3.
14. Sectorització de l'atenció a les persones malaltes amb infart agut de miocardi (IAM) amb elevació del segment ST per tal de portar a terme l'angioplàstia primària. Instrucció 04/2009. CatSalut; 2009.
15. Tubaro M, Danchin N, Goldstein P, Filippatos G, Hasin Y, Heras M, et al. Pre-hospital treatment of STEMI patients. A scientific statement of the Working Group Acute Cardiac Care of the European Society of Cardiology. Acute Card Care. 2011;13:56–67.
16. Bradley EH, Roumanis SA, Radford MJ, Webster TR, McNamara RL, Mattera JA, et al. Achieving door-to-balloon times that meet quality guidelines: how do successful hospitals do it? J Am Coll Cardiol. 2005;46:1236–41.
17. Bradley EH, Curry LA, Webster TR, Mattera JA, Roumanis SA, Radford MJ, et al. Achieving rapid door-to-balloon times: how top hospitals improve complex clinical systems. Circulation. 2006;113:1079–85.
18. Jernberg T, Johanson P, Held C, Svennblad B, Lindbäck J, Wallentin L, et al. Association between adoption of evidence-based treatment and survival for patients with ST-elevation myocardial infarction. JAMA. 2011;305:1677–84.
19. Khot UN, Johnson ML, Ramsey C, Khot MB, Todd R, Shaikh SR, et al. Emergency department physician activation of the catheterization laboratory and immediate transfer to an immediately available catheterization laboratory reduce door-to-balloon time in ST-elevation myocardial infarction. Circulation. 2007;116:67–76.
20. Goldberg RJ, Steg PG, Sadiq I, Granger CB, Jackson EA, Budaj A, et al. Extent of, and factors associated with, delay to hospital presentation in patients with acute coronary disease (the GRACE registry). Am J Cardiol. 2002;89:791–6.
21. Ting HH, Bradley EH, Wang Y, Lichtman JH, Nallamothu BK, Sullivan MD, et al. Factors associated with longer time from symptom onset to hospital presentation for patients with ST-elevation myocardial infarction. Arch Intern Med. 2008;168:959–68.
22. Angeja BG, Gibson CM, Chin R, Frederick PD, Every NR, Ross AM, et al. Predictors of door-to-balloon delay in primary angioplasty. Am J Cardiol. 2002;89:1156–61.
23. Kaul P, Armstrong PW, Sookram S, Leung BK, Brass N, Welsh RC. Temporal trends in patient and treatment delay among men and women presenting with ST-elevation myocardial infarction. Am Heart J. 2011;161:91–7.
24. Curtis JP, Portnay EL, Wang Y, McNamara RL, Herrin J, Bradley EH, et al. The pre-hospital electrocardiogram and time to reperfusion in patients with acute myocardial infarction, 2000-2002: findings from the National Registry of Myocardial Infarction-4. J Am Coll Cardiol. 2006;47:1544–52.
25. Terkelsen CJ, Sørensen JT, Maeng M, Jensen LO, Tilsted HH, Trautner S, et al. System delay and mortality among patients

with STEMI treated with primary percutaneous coronary intervention. JAMA. 2010;304:763–71.
26. Mehta LS, Beckie TM, DeVon HA, Grines CL, Krumholz HM, Johnson MN, et al. Acute myocardial infarction in women: a scientific statement from the American Heart Association. Circulation. 2016;133:916–47.
27. Mehilli J, Kastrati A, Dirschinger J, Pache J, Seyfarth M, Blasini R, et al. Sex-based analysis of outcome in patients with acute myocardial infarction treated predominantly with percutaneous coronary intervention. JAMA. 2002;287:210–5.
28. Hochman JS, Tamis JE, Thompson TD, Weaver WD, White HD, van de Werf F, et al. Sex, clinical presentation, and outcome in patients with acute coronary syndromes. Global Use of Strategies to Open Occluded Coronary Arteries in Acute Coronary Syndromes IIb Investigators. N Engl J Med. 1999;341:226–32.
29. Reina A, Colmenero M, Aguayo de Hoyos E, Arós F, Martí H, Claramonte R, et al. Gender differences in management and outcome of patients with acute myocardial infarction. Int J Cardiol. 2007;116:389–95.
30. Marrugat J, Sala J, Masiá R, Pavesi M, Sanz G, Valle V, et al., RESCATE Investigators. Mortality differences between men and women following first myocardial infarction. JAMA. 1998;280:1405–9.
31. Benamer H, Tafflet M, Bataille S, Escolano S, Livarek B, Fourchard V, et al. Female gender is an independent predictor of in-hospital mortality after STEMI in the era of primary PCI: insights from the greater Paris area PCI Registry. EuroIntervention. 2011;6:1073–9.
32. Lawesson SS, Alfredsson J, Fredrikson M, Swahn E. A gender perspective on short- and long term mortality in ST-elevation myocardial infarction – a report from the SWEDEHEART register. Int J Cardiol. 2013;168:1041–7.