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CARDIOVASCULAR DISEASE

Sex-related differences in prognosis after myocardial infarction: changes from 1978 to 2007

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Abstract Women with myocardial infarction (MI) have shown a 28-day survival disadvantage compared with men. However, results were less consistent when considering long-term mortality in 28-day survivors. The aim was to estimate the trends for sex-related differences in the three endpoints considered for this study: (1) 28-day mortality or severe ventricular dysfunction (acute pulmonary oedema or cardiogenic shock) during the hospital stay, (2) 28-day mortality and (3) two-year cardiovascular mortality or non-fatal MI in 28-day survivors after a first MI. A cohort of 3,982 consecutive patients with first Q-wave MI admitted to a university tertiary reference hospital between 1978 and 2007 was followed for 2 years. Short-term prognosis improved in women over the studied period; similar rates were observed in both sexes in the 2000s. After adjusting for age, co-morbidities and anterior location of MI, female sex had an odds ratio = 1.71 (95 % confidence interval [CI] 1.34–2.17) of short-term severe MI or death over the studied period. Overall, sex differences in long-term prognosis remained similar over the studied period (hazard ratio = 1.40; 95 % CI 1.02–1.91). In conclusion, short-term prognosis improved over the past 30 years for first Q-wave MI patients, becoming similar for both men and women in the most recent decade. Long-term prognosis did not improve in either men or women, indicating that secondary prevention should be reinforced to achieve consistent reductions in the number of cardiovascular events.

Keywords Cohort study · Coronary disease · Epidemiology · Myocardial infarction · Prognosis · Sex

Abbreviations

ACE	Angiotensin-converting enzyme
CABG	Coronary artery bypass graft surgery
CHD	Coronary heart disease
HR	Hazard ratio
MI	Myocardial infarction

This study is conducted on behalf of the REGICOR Investigators.

See the roster of REGICOR Investigators at: www.regicor.org/regicor_inv.

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OR Odds ratio
PCI Percutaneous coronary intervention

Introduction

Coronary heart disease (CHD) population mortality rates experienced a profound secular decline during the last three decades of the twentieth century, particularly in western countries [1]. Most of this change can be attributed to improvement in modifiable lifestyle and cardiovascular risk factors [2]. In addition, cardiovascular treatments developed since 1980 have contributed to increase life expectancy in CHD patients [3]. Hence, in-hospital mortality has significantly decreased in both sexes, concurring with changes in the treatment of myocardial infarction (MI) patients and regardless of the severity of patients admitted to hospitals [4–6].

Greater mortality in women as compared to men with acute MI is consistently observed in the medical literature [7–14]. Mechanisms implicated in the excess risk of short–term mortality have not been conclusively established but include more frequent reinfarctions and procedural complications, older age and greater co-morbidity (e.g., diabetes and hypertension) in women than in men [15–17]. On the other hand, less consistent results were observed in long-term mortality. Although significantly higher rates of death, reinfarction and ventricular dysfunction were observed in women [7, 18], other studies have reported long-term mortality to be similar between sexes in acute-phase survivors [12, 19].

The secular analysis of the population-based registry of consecutive MI patients in Girona since 1978 provides a good opportunity to identify the progress in MI prognosis and to test whether the accumulated knowledge on sex-related differences resulted in any improvement in prognosis or more intensive management of women.

The aim of this study was to estimate the trends in the 30-year period from 1978 to 2007 for sex-related differences in the three endpoints considered for this study: (1) 28-day mortality or severe ventricular dysfunction (acute pulmonary oedema or cardiogenic shock) during the hospital stay, (2) 28-day mortality and (3) two-year cardiovascular mortality or non-fatal MI in 28-day survivors after a first MI.

Methods

Patient population

This cohort study included 3,982 consecutive patients, residents of Girona (Spain) aged 25–74 years, admitted with first Q-wave MI to one single tertiary referral university hospital between 1978 and 2007 [3, 20]. In this setting, six community hospitals refer MI patients after emergency treatment, which provides a population-based registry of hospitalized MI patients in a 591,060 km^2 region of northeast Spain with approximately 600,000 inhabitants. The study protocol was approved by the local ethics committee and all research was conducted in accordance with the Declaration of Helsinki rules of the World Medical Association.

Myocardial infarction definition

The diagnosis of Q-wave MI was made when abnormal new Q- or QS-waves appeared in serial electrocardiograms and at least one of two other criteria were met: typical chest pain lasting 20 min or more for which no cause other than CHD was found, and at least twice the upper normal level of MI necrosis enzymes. To ensure consistent diagnosis over the long study period, the only markers of myocardial necrosis considered were creatine phosphokinase greater than twice the upper normal value, myocardial fraction of total creatine phosphokinase more than 10 %, or both; troponin was not considered.

According to the current and classical guidelines [21], the presence of a pathological Q-wave related to MI was considered if we observed at least one of the following three conditions: (1) any Q-wave of 0.02 s or more or QS complex in leads V2–V3; (2) Q-wave of 0.03 s or more and more than 0.1 mV deep or QS complex in any 2 leads of a contiguous lead grouping of leads I, II, aVL, aVF, or V4–V6 (I, aVL, V6; V4–V6; II, III and aVF); and (3) R-wave of 0.04 s or more in V1–V2 and R/S of 1 or more with a concordant positive T-wave in the absence of a conduction defect.

Patients with a pacemaker and bundle branch block rhythm that made ECG location of MI impossible were also included in this analysis (37 cases).

Variables collected

All variables in the study (sociodemographics, co-morbidity, MI severity and patient management) were prospectively collected by a trained team of nurses. Sex, age, previous history of smoking, diabetes, hypertension and angina were self-reported. Clinical variables (systolic and diastolic blood pressure, glycaemia), treatments and procedures were collected from medical records. We considered a patient diabetic when he/she reported previous diagnosis or treatment or when the diagnosis was done during a hospital stay with two consecutive fasting glycaemia determinations above the recommended threshold in the corresponding period (i.e., 140 mg/dl until 1998 and

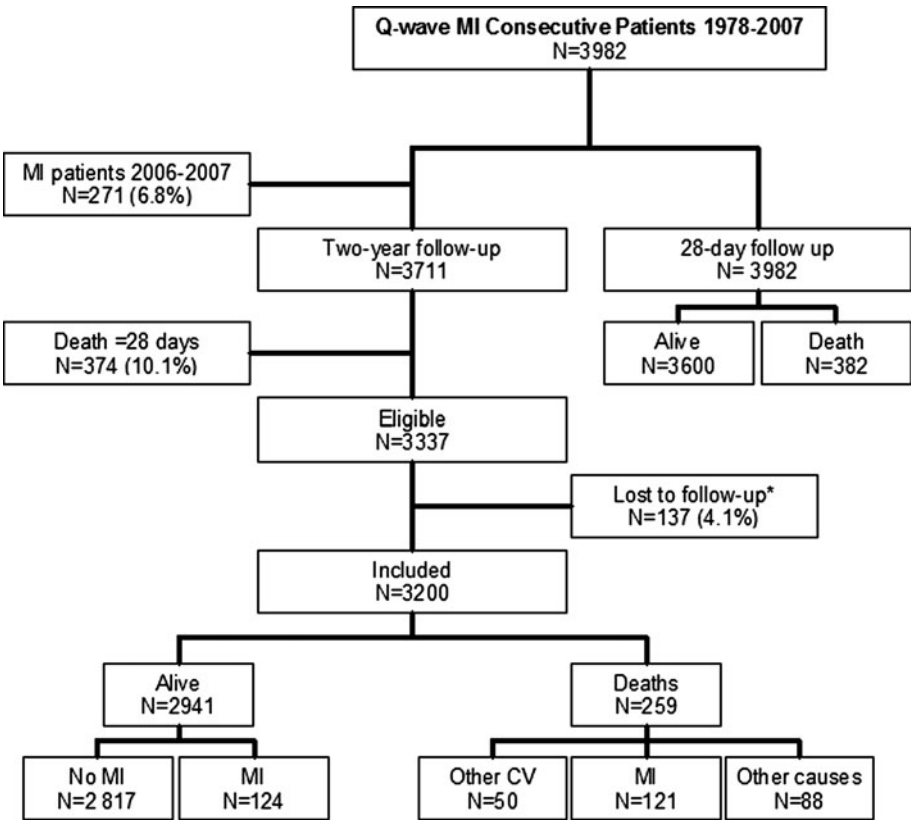

Fig. 1 Participation and follow-up flow chart. *CV* cardiovascular, *MI* Myocardial infarction. *Not found by telephone contact, mortality registry or myocardial infarction registry

126 mg/dl after 1998). Hypertension was considered when a patient reported previous diagnosis or treatment, or when abnormal blood pressure values according to Joint National Committee criteria were detected after 5 min rest once the patient's hemodynamic status was stable. Blood pressure was measured at least twice (48 h after admission and 24 h before discharge) in the tertiary hospital. Two blood pressure measurements were taken and the mean value was recorded for the study. The cut-off points considered for the diagnosis of both diabetes and hypertension changed during the study period as changes occurred in established recommendations. History of previous angina was considered when the patient reported previous diagnosis or treatment or, alternatively, when typical chest pain lasting less than 20 min was reported to exist in the 48 h prior to MI symptom onset. Elapsed time from onset of symptoms to hospital admission was collected in 40 % of the sample.

Disease severity was established by anterior MI location on diagnostic electrocardiogram and ventricular arrhythmias (fibrillation or tachycardia) occurring within the first 48 h after MI and requiring immediate treatment. Collection of management variables was regularly updated to include thrombolysis, anti-platelet drugs, β-blockers, angiotensin-converting enzyme (ACE) inhibitors, coronary angiogram, percutaneous coronary intervention (PCI) and coronary artery bypass graft surgery (CABG) as appropriate.

Follow-up and end-points

To ensure that all patients would have similar long-term follow-up we included all participants from 1978 to 2007 for 28-day follow-up, but considered only those admitted from 1978 to 2005 for two-year follow-up analysis. The three end-points were: (1) mortality or severe ventricular dysfunction, defined as occurrence of acute pulmonary oedema (sudden onset of orthopnoea, inspiratory rales, documented hypoxemia and alveolar and/or interstitial pulmonary oedema at the chest X-ray) or cardiogenic shock (hypotension, measured as systolic blood pressure lower than 90 mmHg, and evidence of peripheral vasoconstriction -oliguria, cyanosis or sweating) during the hospital stay; (2) 28-day mortality; and (3) two-year cardiovascular mortality or non-fatal MI in 28-day survivors of a first MI. Short-term mortality was considered cardiovascular in all instances. Long-term endpoint was non-fatal MI or cardiovascular mortality at two years for 28-day survivors included from 1978 to 2005. Patients were followed in the outpatient clinic or by telephone contact. Cause of death was ascertained by reviewing medical records or, in cases of out-of-hospital death, clinical records and death certificates in the Catalonia Death Registry. The criteria for non-fatal MI during follow-up were identical to those for the index event. Follow-up for 28-day and two-year mortality was 100 % in patients

Table 1 Patient characteristics, drug procedure used and outcomes by sex

	Men (n = 3,307)	Women (n = 675)	*P*
Age, mean (SD)	59 (10)	65 (8)	<0.001
Diabetes, n (%)	651 (20.5)	289 (43.9)	<0.001
Hypertension, n (%)	1,400 (43.6)	418 (63.0)	<0.001
Smokers, n (%)	2,067 (63.4)	78 (11.8)	<0.001
Previous angina, n (%)	1,393 (43.3)	317 (48.8)	0.011
Anterior MI ECG location, n (%)	1,435 (43.6)	318 (47.7)	0.060
APO/CS, n (%)	361 (11.0)	167 (25.0)	<0.001
Ventricular arrhythmia, n (%)	439 (13.6)	74 (11.2)	0.121
Thrombolysis, n (%)	1,094 (33.4)	166 (24.9)	<0.001
Anti-platelet drugs, n (%)	2,114 (64.9)	432 (65.3)	0.898
β-blockers, n (%)	1,195 (36.7)	220 (33.1)	0.081
ACE inhibitors, n (%)	873 (26.5)	184 (27.3)	0.696
28-day angiograms, n (%)	774 (23.4)	167 (24.7)	0.487
28-day PCI, n (%)	413 (35.7)	73 (29.8)	0.093
28-day CABG, n (%)	66 (2.0)	15 (2.2)	0.818
Angina post-MI, n (%)	352 (16.0)	111 (23.7)	<0.001
28-day mortality, n (%)	274 (8.3)	108 (16.0)	<0.001
Severe ventricular dysfunction or 28-day mortality, n (%)	479 (14.5)	204 (30.2)	<0.001
Two-year CV mortality, n (%)	86 (3.1)	35 (6.7)	<0.001
Two-year CV mortality or non-fatal MI[a], n (%)	230 (8.2)	76 (14.5)	<0.001

ACE angiotensin-converting enzyme, *APO/CS* acute pulmonary oedema/cardiogenic shock, *CABG* coronary artery bypass grafting, *CV* cardiovascular, *ECG* electrocardiography, *MI* myocardial infarction, *PCI* percutaneous intervention, *SD* standard deviation

[a] 1998–2005 for 2-year outcomes

diagnosed between 1978 and 2005, and was 95.9 % for MI at 2 years in 28-day survivors (Fig. 1).

Statistical analysis

The 683 cases of severe ventricular dysfunction or death observed at 28 days among the 3,982 included patients (17 % women) provided 80 % power to detect an adjusted odds ratio (OR) $\geq$1.3 that women would develop an event at 28 days, assuming the event rate in men to be 14.5 %, the proportion of women in the sample 17 %, the correlation of sex with potential confounders (up to 7 covariates) approximately 0.50 or lower and a *P* value of 0.05.

Age was summarized as mean and standard deviation, and categorical variables as proportions. Chi-square test for categorical variables and Student *t* test for continuous variables were computed to test sex-related differences in co-morbidity, disease severity, MI management and event rate during follow-up. The same tests were used as appropriate to assess the differences in sociodemographic, co-morbidity, disease severity and MI management variables according to event occurrence during follow-up.

Two logistic regression models were fitted for short-term prognosis endpoints, adjusting for age, sex, disease severity (MI location), co-morbidity (hypertension, diabetes, smoking, previous angina) and year of inclusion in the registry. A Cox proportional hazard model was used to fit models for long-term prognosis (two-year cardiovascular mortality or non-fatal MI in 28-day survivors) with similar stratification and adjustment as for the 28-day period in a logistic regression model. For each participant, probabilities were calculated for the three different outcomes considered in the follow-up: (1) severe ventricular dysfunction during hospital stay or 28-day mortality, (2) 28-day mortality and (3) two-year cardiovascular mortality or non-fatal MI in 28-day survivors). The results were plotted by year in a smoothed spline regression adjusted for age, sex, disease severity (myocardial infarction location), co-morbidity (hypertension, diabetes, smoking, previous angina) and year of inclusion in the registry.

Calculations were made with R statistical package (R Foundation for Statistical Computing, Vienna, Austria; version 2.14.1).

Results

In total, 3,982 participants were included (17 % women) between 1978 and 2007. Mean age, previous history of diabetes, hypertension and angina was significantly higher in women, whereas men were more often smokers. One of 4 women presented with severe ventricular dysfunction (acute pulmonary oedema or cardiogenic shock) after MI, whereas this figure was significantly lower in men (11 %). Regarding MI management, we did not observe significant differences except for greater use of thrombolysis in men. Short- and long-term prognosis after MI was much worse in women compared to men in the period considered in the unadjusted analysis (Table 1). Finally, women arrived at the hospital significantly later after symptoms onset than men (150 vs. 120 min, respectively, $P < 0.001$).

Men and women with worse short- and long-term prognosis were significantly older, had higher prevalence of diabetes and hypertension, and were less often smokers. Additionally, men and women with severe or fatal MI were less often treated with proven-efficacy drugs and PCI during the MI acute phase, and had a higher proportion of anterior MI and ventricular arrhythmia. On the other hand, both men and women who survived the first 28 days were more likely to experience non-fatal MI or death within 2 years if they had previous history of angina, reinfarction or post-MI angina during admission, acute pulmonary

Table 2 Characteristics of patients aged 25–74 years with a first Q-wave myocardial infarction admitted between 1978 and 2007 by endpoint: severe ventricular dysfunction or death at 28 days and 2-year cardiovascular death or non-fatal MI

	Short-term prognosis			Long-term prognosis		
	Severe ventricular dysfunction or 28-day mortality			Two-year CV mortality or non-fatal MI		
	No (n = 3,273)	Yes (n = 683)	*P*	No (n = 2,894)	Yes (n = 306)	*P*
Age, mean (SD)	59 (10)	64 (8)	<0.001	59 (10)	63 (9)	<0.001
Women, n (%)	468 (14.3)	204 (29.9)	<0.001	429 (14.8)	76 (24.8)	<0.001
Diabetes, n (%)	682 (21.5)	250 (38.8)	<0.001	640 (22.8)	95 (32.5)	<0.001
Hypertension, n (%)	1,450 (45.2)	361 (55.4)	<0.001	1,259 (44.4)	166 (56.1)	<0.001
Smokers, n (%)	1,850 (57.0)	279 (42.3)	<0.001	1,625 (56.7)	142 (47.3)	0.002
Previous angina, n (%)	1,379 (43.1)	323 (50.2)	0.001	1,200 (42.5)	158 (53.7)	<0.001
Anterior MI, n (%)	1,359 (41.6)	385 (57.7)	<0.001	1,226 (42.5)	144 (47.4)	0.102
APO/CS, n (%)	–	–	–	211 (7.3)	57 (18.9)	<0.001
Ventricular arrhythmia, n (%)	309 (9.6)	204 (31.0)	<0.001	308 (10.8)	41 (13.9)	0.111
Thrombolysis, n (%)	1,114 (34.3)	139 (20.7)	<0.001	953 (33.2)	72 (23.8)	0.001
Anti-platelet drugs, n (%)	2,138 (66.1)	393 (59.1)	0.001	1,829 (64.0)	186 (61.6)	0.412
β-blockers, n (%)	1,312 (40.5)	95 (14.4)	<0.001	982 (34.3)	79 (26.2)	0.004
ACE inhibitors, n (%)	885 (27.1)	166 (24.6)	0.208	673 (23.3)	73 (23.9)	0.830
28-day angiograms, n (%)	790 (24.1)	146 (21.4)	0.135	613 (21.2)	58 (19.0)	0.363
28-day PCI, n (%)	433 (36.5)	51 (24.5)	0.001	271 (10.5)	23 (8.6)	0.308
28-day CABG, n (%)	58 (1.8)	23 (3.4)	0.011	62 (2.1)	5 (1.6)	0.555
Angina post-MI, n (%)	369 (16.6)	92 (21.1)	0.028	357 (18.7)	48 (25.4)	0.025
Reinfarction, n (%)	63 (2.8)	25 (5.7)	0.004	56 (2.0)	16 (5.4)	<0.001

ACE angiotensin converting enzyme, *APO/CS* acute pulmonary oedema/cardiogenic shock, *CABG* coronary artery bypass grafting, *MI* myocardial infarction, *PCI* percutaneous intervention

oedema or cardiogenic shock, and had received neither thrombolysis nor β-blockers (Table 2).

Throughout the whole study period, the adjusted OR for 28-day severe or fatal MI for women compared with men was 1.71 (95 % confidence interval [CI] 1.34–2.17); for fatal MI specifically, the adjusted OR was 1.33 (95 % CI 0.97–1.82) (Table 3). However, short-term prognosis improved in women over the studied period more rapidly than in men after adjusting for potential confounders. Indeed, the steady decrease in 28-day mortality led to similar rates for women and men in the 2000s. Sex-related differences in severity of MI also decreased over that period; however, a small gap remained for the combined endpoint in 2007 (Fig. 2a, b). On the other hand, the hazard ratio (HR) for two-year cardiovascular mortality or non-fatal MI was 1.40 (95 % CI 1.02–1.91) because adjusted sex-related differences in long-term prognosis remained similar throughout the 30 years studied (Table 4, Fig. 2c).

Discussion

Short-term prognosis after MI has improved in both sexes in the past 30 years, but on a steeper curve in women than in men; as a result, the gap between sexes has narrowed. This significant decrease in short-term mortality may have averted a number of deaths in the acute phase of MI and delayed them within the succeeding 2 years. Indeed, the long-term event rate has only slightly decreased during the past 30 years, with women still at higher risk to suffer cardiovascular events. Thus, more intensive secondary prevention is probably indicated if we are to achieve a long-term decrease in recurrences.

Sex-related differences in short-term and long-term prognosis

The reasons why MI poses a greater threat for women than for men are not entirely clear. The existence of true sex-related differences in mortality after MI or whether they are due to older age or higher prevalence of co-morbidities have been extensively debated [16, 17, 19]. Several studies concluded that not only did differences in the prevalence of diabetes make women more vulnerable, but that this disease may induce a more unfavourable cardiovascular risk profile among women compared to men [2, 22]. Our study showed the excess short-term risk of severe or fatal MI in women to be only partially explained by age, diabetes,

Table 3 Univariate odds ratio (OR), and that adjusted by multivariate logistic regression analysis, of severe ventricular dysfunction (acute pulmonary oedema or cardiogenic shock) during hospital stay or 28-day mortality and the 28-day mortality for women and by clinical characteristics of patients with first Q-wave myocardial infarction (n = 3,982)

	Severe ventricular dysfunction or 28-day mortality						28-day mortality					
	Crude OR	95 % CI for OR	*P* value	Adjusted OR	95 % CI for OR	*P* value	Crude OR	95 % CI for OR	*P* value	Adjusted OR	95 % CI for OR	*P* value
Sex (female)	2.55	(2.11–3.09)	<0.001	1.71	(1.34–2.17)	<0.001	2.11	(1.66–2.68)	<0.001	1.33	(0.97–1.82)	0.072
Age	1.07	(1.06–1.08)	<0.001	1.06	(1.04–1.07)	<0.001	1.08	(1.06–1.09)	<0.001	1.08	(1.06–1.09)	<0.001
Diabetes	2.31	(1.93–2.77)	<0.001	1.83	(1.50–2.25)	<0.001	1.68	(1.33–2.12)	<0.001	1.30	(0.99–1.71)	0.061
Hypertension	1.50	(1.27–1.78)	<0.001	1.22	(1.01–1.48)	0.038	1.38	(1.11–1.72)	0.004	1.19	(0.93–1.53)	0.162
Smoking	0.55	(0.47–0.65)	<0.001	1.10	(0.88–1.37)	0.410	0.51	(0.41–0.64)	<0.001	0.83	(0.62–1.11)	0.208
Previous angina	1.33	(1.12–1.57)	0.001	1.13	(0.94–1.36)	0.197	1.43	(1.15–1.78)	0.001	1.16	(0.91–1.48)	0.243
Anterior MI ECG location	1.92	(1.62–2.27)	<0.001	1.97	(1.63–2.38)	<0.001	1.91	(1.53–2.37)	<0.001	1.80	(1.40–2.30)	<0.001
Year	0.98	(0.97–0.99)	0.002	0.98	(0.97–0.99)	0.005	0.95	(0.94–0.96)	<0.001	0.94	(0.92–0.96)	<0.001

Models are adjusted for age, sex, disease severity (MI location), co-morbidity (hypertension, diabetes, smoking, previous angina) and year of inclusion

ECG electrocardiogram, *MI* myocardial infarction

hypertension or anterior location of MI. Vaccarino et al. pointed out that true sex-related differences were confined to younger age strata in the US population [23, 24]. However, we could not confirm this hypothesis in our low incidence area where MI in women younger than 60 is rare [4], less than 25 % in our sample.

After 2000, the gap in short-term mortality between men and women declined to the point that after 2008 any differences were not significant. This decrease may have had an effect on the stabilization of the long-term incidence of cardiovascular events in 28-day survivors. Sex-related differences at long-term, already described in previous studies [7, 12, 19], were confirmed in our work. In addition to female sex, the risk factors associated with poor prognosis were age, diabetes, hypertension and previous angina. Therefore, secondary prevention should be intensified to achieve consistent reductions in the number of recurrent events in women.

Global decline in coronary heart disease mortality

Declining in-hospital mortality has contributed to the steep decrease in CHD mortality observed in western countries since 1970 [1]. Improvements in MI management have been traditionally associated with a decrease in the percentage of in-hospital deaths. Most time-trend studies have attributed such a decrease to proven-efficacy treatments and procedures [3, 4, 25–28]. Previous studies have underlined that women with acute coronary syndrome are less intensively treated than men [29, 30]. To understand delays in ECG acquisition and explain under-treatment, the authors of these studies pointed to diagnostic uncertainty because MI is less frequent in women, physicians may fail to recognize the atypical symptoms of MI that are more prevalent in women than in men, and women may discount or underreport MI symptoms [30–32]. In addition, women with MI took about half an hour longer than men to arrive to the referral hospital in the present study. However, treatment use was similar in men and women in our study, except for thrombolysis, which was significantly less often used in women.

A recent publication reported that 47 % of CHD mortality decline in Spain can be attributed to acute phase MI management and 50 % to primary prevention, respectively [33]. These results reinforced the role of primary prevention in the reduction of CHD incidence, severity and mortality. In fact, our study suggests that diabetes and hypertension are important determinants of worse short- and long-term outcomes. Consequently, the observed changes in the prevalence of obesity, closely related to diabetes incidence [34], in our region in the last decade might translate into higher MI incidence, mortality rates and event severity in the near future [35].

Fig. 2 Changes by sex in the probability of severe ventricular dysfunction or 28-day in-hospital mortality (**a**), 28-day in-hospital mortality (**b**) and two-year mortality or non-fatal myocardial infarction (**c**) from 1978 to 2007. The spline models were adjusted for age, sex, disease severity (myocardial infarction location) and co-morbidity (hypertension, diabetes, smoking and previous angina)

Table 4 Univariate relative risk (RR) and multivariate Cox proportional model for the hazard ratio (HR) of two-year cardiovascular mortality or non-fatal myocardial infarction by clinical characteristics of patients with first Q-wave myocardial infarction in 28-day survivors of a first myocardial infarction (n = 3,200)

	Crude RR	95 % CI for RR	*P* value	Adjusted HR	95 % CI for HR	*P* value
Sex (female)	1.85	(1.43–2.40)	<0.001	1.40	(1.02–1.91)	0.035
Age	1.04	(1.03–1.05)	<0.001	1.03	(1.02–1.05)	<0.001
Diabetes	1.62	(1.27–2.07)	<0.001	1.34	(1.03–1.74)	0.030
Hypertension	1.58	(1.26–1.99)	<0.001	1.39	(1.09–1.78)	0.008
Smoking	0.68	(0.54–0.85)	0.001	1.05	(0.79–1.39)	0.728
Previous angina	1.55	(1.24–1.95)	<0.001	1.43	(1.12–1.81)	0.004
Anterior MI ECG location	1.22	(0.97–1.53)	0.086	1.17	(0.92–1.48)	0.204
Year	0.99	(0.98–1.01)	0.262	0.99	(0.97–1.01)	0.195

Models are adjusted for age, sex, disease severity (myocardial infarction location), co-morbidity (hypertension, diabetes, smoking and previous angina) and year of inclusion

ECG electrocardiogram, *MI* myocardial infarction

Strengths and limitations

The REGICOR Project is an industry-free MI registry created to ascertain the role of protective factors in Southern Europe that determine the low MI incidence observed. To guarantee the representativeness of the sample, consecutive recruitment of patients admitted to a tertiary hospital in an area in North-eastern Spain and aged 25–74 years was adopted. Indeed, the 28-day hospital case-fatality reduction over time in our study was also observed in individuals with ST-segment elevation MI (STEMI) in the joint analysis of PRIAMHO I, PRIAMHO II and the MASCARA Spanish multi-centre registries [36]. In addition, previous studies have shown that the variability in MI incidence and population case-fatality rate was relatively low in Spanish autonomous communities [37, 38]. Although our results cannot be generalized to other Spanish regions it is logical to expect relatively similar results in MI prognosis in similar socio-economic and health care contexts. For consistency of analysis over the long study period, this study did not include individuals older than 74 years, who now constitute a much larger proportion of all patients with MI.

In the context of the REGICOR Project, the MI population registry covers events from 1990 to date. Approximately 67 % of the patients aged 25–74 years who lived in the area and were diagnosed with first Q-wave MI between 1990 and 2006 were admitted to Dr Josep Trueta Hospital. The mean age was 60 years and 20 % of these patients were women. Since the present study included data from a hospital MI registry, it did not consider out-of-hospital deaths. However, a previously published analysis of the REGICOR population registry found a significantly higher population case-fatality rate in women compared to men (45 vs. 42 %) between 1990 and 1999 [5]. The dramatic decrease in case fatality observed in the 21st century has

led to a similar proportion for both sexes (20 %) [data not published].

Since 2000, troponin values have also been used to clinically define MI cases in the REGICOR catchment area. However, to be consistent throughout the studied period, creatine phosphokinase was the only myocardial necrosis marker used in MI definition by REGICOR. Although the reference values of this enzyme have changed over time, the stable criterion was to consider abnormal those determinations above twice the upper limit of the reference values.

Conclusion

Short-term prognosis has been worse overall in women than in men with first Q-wave MI patients over the past 30 years, but has improved faster in women to the point that it resembles that of men since 2007. On the other hand, long-term prognosis did not improve over the studied period in men or women, indicating that secondary prevention should be reinforced to achieve a success similar to the short-term prognosis.

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Conflict of interest None.

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