HIGHLIGHTS

- In patients with STEMI, sex and prior CVD had a synergistic impact on mortality.
- Compared to men, women had a similar prognosis in patients without CVD.
- Compared to men, women had lower mortality risk among those with prior CVD.
- In addition to an interaction, the study illustrates the index event bias phenomenon.
- In a selected cohort with previous CVD, female sex becomes a "protective" factor.

ABSTRACT

Background: Sex and prior cardiovascular disease (CVD) are known independent prognostic factors following an ST-elevation myocardial infarction (STEMI). We aimed to examine whether the association between sex and 30-day mortality differ according to the presence of previous CVD in STEMI patients.

Methods: Prospective, observational, multicentre registry of consecutive patients managed in 17 STEMI networks in Spain (83 centres), between April and June 2019. Unadjusted and adjusted logistic regression models assessed the association of 30-day mortality with sex and prior CVD status, as well as their interaction.

Results: Among 4366 patients (mean age 63.7±13.0 years; 78% male), there were 337 (8.1%) deaths within the first 30 days. There was an association between crude 30-day mortality and sex (women 10.4% vs. men 7.4%, p=0.003), and prior CVD (CVD 13.7% vs non-CVD 6.8%, p<0.001). After adjustment for potential confounding, neither sex nor prior CVD were apparently associated with mortality. Nevertheless, we found a significant sex-CVD interaction (p-interaction=0.006), since women were at lower risk than men in the subset of patients with prior CVD (OR=0.30, 95%CI=0.12-0.80) but not in those without CVD (OR=1.17, 95%CI=0.79-1.74).

Conclusions: Women as well as patients with prior CVD have an increased crude risk of 30-day mortality. However, sex-related differences in short term mortality are modulated by the interaction with CVD in STEMI patients. Compared to men, women had a similar prognosis in the subset of patients without CVD, whereas they were associated with a lower risk of mortality among those with prior CVD after adjusting for other prognostic factors.

Keywords: ST Elevation Myocardial Infarction; Cardiovascular Disease; Women, Mortality; Prognosis.

Short-term mortality differs between men and women according to the presence of previous cardiovascular disease: insights from a nationwide STEMI cohort

Running head: Impact of Sex and Cardiovascular Disease in STEMI

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◊ See the appendix for details on the institutions and organizations that participated in the Infarction Code Working Group of the Interventional Cardiology Association of the Spanish Society of Cardiology.

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KEYWORDS

ST Elevation Myocardial Infarction; Cardiovascular Disease; Women, Mortality; Prognosis.

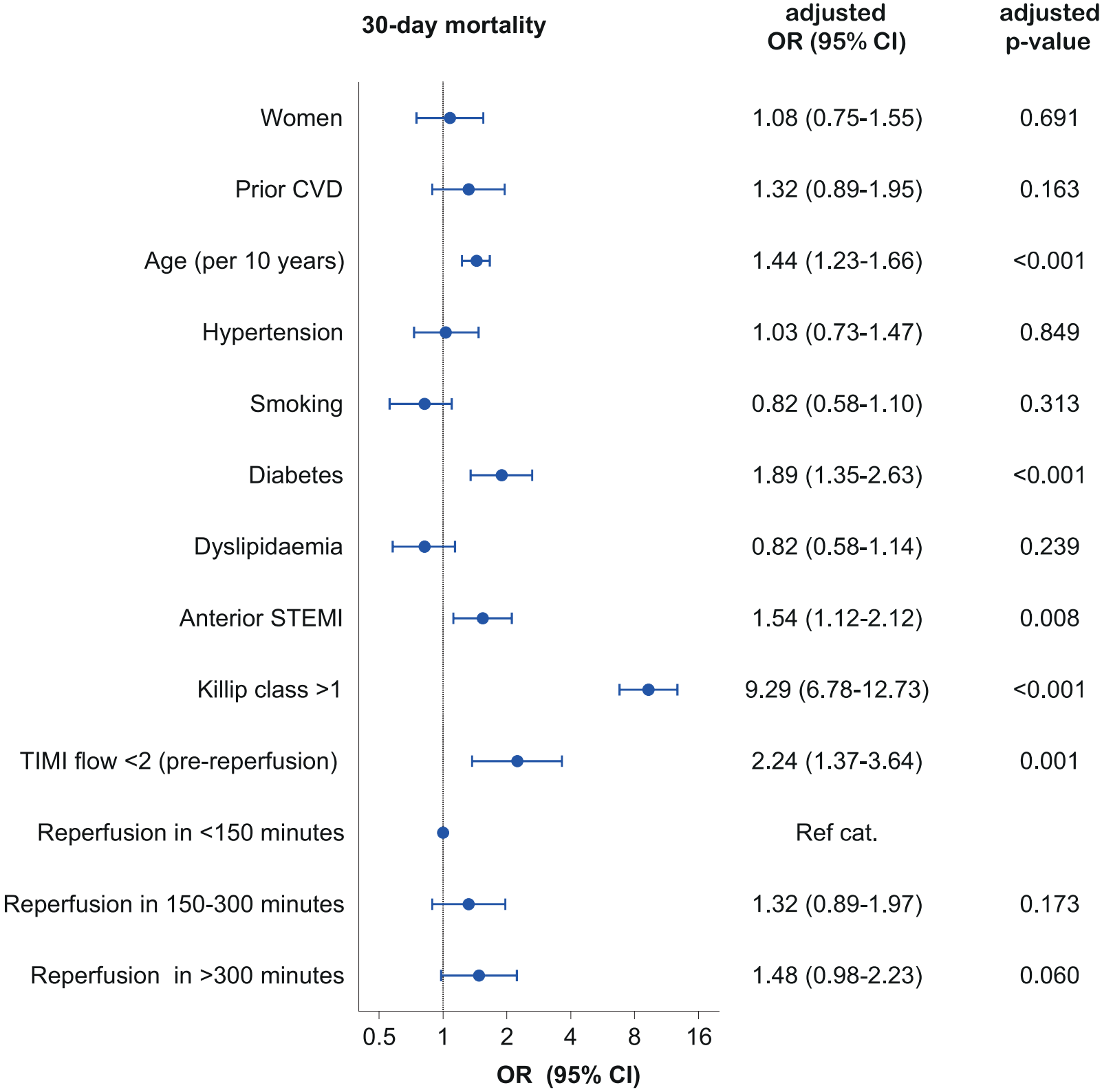
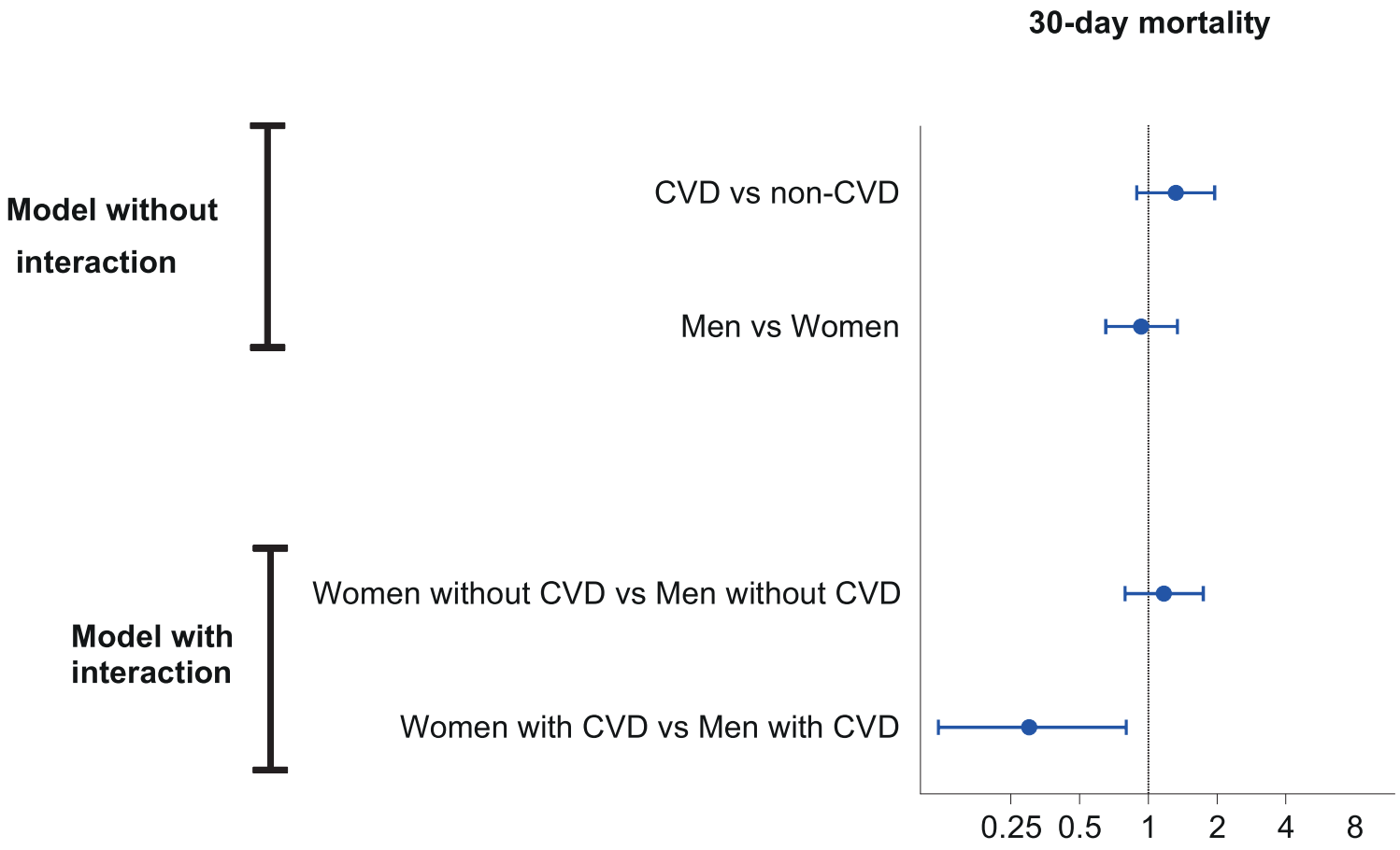


Figure 2

A Thirty-day all-cause mortality by sex, according to prior CVD status

Patients with prior CVD (n=670)				
	Overall	**No. Deaths**		**p-value**
Men	552	79	14.31%	0.345
Women	118	13	11.02%	
Patients without prior CVD (n=3347)				
	Overall	**No. Deaths**	**30-day Mortality (%)**	**p-value**
Men	2588	153	5.91%	<0.001
Women	759	76	10.01%	

B Assessment of the interaction between sex and prior CVD in multivariate adjusted models



INTRODUCTION

Acute myocardial infarction (AMI) is a leading global cause of death in both men and women[1]. Among others, sex and prior cardiovascular disease (CVD) are known determinants of survival following AMI[2,3]. Although women are less likely to survive after an AMI than men[4–6], their poor prognosis is likely to be confounded by differences in baseline cardiovascular risk factors, age and clinical management, since women tend to have more comorbidities and receive less often coronary revascularization and guideline-based therapies at discharge[7]. Some studies have shown that, after adjustment for them, the risk of all-cause death after discharge was actually lower in women in comparison to men[8].

Patients with CVD in any of their clinical forms across the atherosclerotic disease continuum, such as AMI or stroke, are at higher risk of presenting a recurrent cardiovascular event[9,10]. However, in hospital mortality has been similar between those with or without previous CVD[11–13]. It has been suggested that short term outcomes in AMI are less determined by the patient risk profile, and more by the clinical features of their presentation, such as the immediate reperfusion and the Killip class[14].

There are limited data available regarding the synergistic impact of sex and prior CVD on short term mortality in patients with ST-elevation myocardial infarction (STEMI). Our main hypothesis was that the association between sex and mortality may differ according to the presence of previous CVD. Moreover, women with STEMI might have a worse prognosis than men in the index episode, but they might seem to be "protected" in the presence of a recurrent episode because of the index event bias. Similar to what happens with the obesity paradox (obesity is an established risk factor for coronary artery disease but appears to protect against recurrent coronary events)[15], the association between sex and mortality might represent another example of a cardiovascular paradox. Because of the general congruence between risk factors for the index and recurrent events, the so called "index event bias" underestimates, or even reverses, some associations[16].

Using data from a prospective, observational, multicentre cohort of consecutive STEMI patients recruited in 83 Spanish hospitals[17] we aim to: (a) evaluate the association between sex and mortality; (b) assess the association between previous CVD and mortality; (c) illustrate the presence of an index event bias using a "selected" population with previous CVD; and (d) determine whether the association between sex and mortality may vary based on the presence of previous CVD (i.e., testing for interaction).

METHODS

Setting and Design

The Interventional Cardiology Association of the Spanish Society of Cardiology (ACI-SEC) conducted a prospective registry of consecutive patients with suspected STEMI who were managed by any of the 17 regional STEMI care networks from Spain. They involve 83 hospitals capable of performing primary percutaneous coronary interventions in year-round 24-hour, 7-days a week program[17]. Data regarding patient demographics, medical history, early medical management, and acute reperfusion therapies were collected during the index STEMI admission at each hospital. The research protocol was approved by the Working Group on STEMI Code of the Spanish Interventional Cardiology Association. Because of the acute setting and patient data collection was performed anonymously, institutional review boards waived the need for individual informed consent.

Patient population

Between April and June 2019, 5401 with suspected STEMI were managed by the STEMI networks. Patients without a confirmed diagnosis STEMI were excluded from this analysis. Participants were categorized by sex, and by the presence of previous CVD. Previous CVD was defined as the presence of prior diagnosis of AMI, prior percutaneous coronary revascularization (PCI), history of coronary artery bypass grafting (CABG), or prior diagnosis of stroke. The primary outcome was 30-day all-cause mortality, which was collected locally in each hospital.

Statistical analysis

Categorical variables are presented as frequency and percentage, whereas continuous variables are summarized as mean (SD) or median (interquartile range, IQR), as appropriate. Comparisons between groups were performed using chi-square tests, t tests or Mann-Whitney U tests, as appropriate. The association between the study variables (sex and previous CVD) and the outcome (30-day mortality) was initially estimated using a logistic regression model for each study variable, which yielded odds ratios (ORs) with their corresponding 95% confidence interval (95% CI).

Multivariate logistic regression modelling was performed to address any potential confounding[18,19]. Based on clinical judgment and the findings of univariate associations, the following covariates were included in multivariate models: age, hypertension, diabetes, dyslipidaemia, smoking status, time from pain onset to reperfusion, anterior MI, Killip class, and baseline TIMI flow. In order to evaluate changes in the association between sex and mortality due to a potential index-event bias, our cohort was split based on the presence of previous CVD. Estimates from a multivariate regression model conditioned on previous CVD (selected population) were then compared to the estimates yielded by the multivariate regression model using the whole cohort (unselected population).

Further analyses were carried out to examine the potential interaction between sex and CVD by introducing the term "s*ex x CVD"* into the multivariate model and testing for their statistical significance through the likelihood ratio test. Percentages of missing values according to sex are presented in Supplementary **Table S1**. To account for missing covariates, a multiple imputation technique was applied using chained equations (30 imputed data sets was used), which was used to confirm the findings of the model with the interaction term (s*ex x CVD*). The estimates from each imputed dataset were combined using Rubin's rules. All p-values were 2-sided and values of <0.05 were considered as significant. All statistical analyses were performed

using STATA software, version 16.1 (Stata Corp, College Station, TX, USA). GraphPad Prism version 6.00 (GraphPad Software, La Jolla California) was used to produce the figures.

RESULTS

Baseline Characteristics and STEMI management

A total of 5401 patients from 83 Spanish hospitals were enrolled in the registry. After excluding 1035 patients with other diagnosis than STEMI, 4366 were included in the current study, with a mean age of 63.7±13.0 years. There were 3403 (78.0%) men, and 691 (16.4%) patients with previous CVD. Baseline clinical features, medical STEMI management, and outcomes by sex and prior CVD status are shown in **Table 1** and **Table 2**, respectively.

Women with STEMI were significantly older (mean age 69.5±13.3 *vs.* 62.0±12.4 years, p<0.001), had more frequently hypertension (57.9% *vs.*49.0%, p<0.001), but lower prevalence of smoking (30.8% *vs.*48.3%, p<0.001) in comparison to men. Women presented with Killip class higher than I more frequently than men (22.2% *vs.* 17.5%, p<0.001), as well as longer pain-to-balloon delays (214 [141-368] *vs.* 195 [135-320] minutes, p=0.039). There was no difference in terms of culprit vessel by sex. However, women were less likely to receive primary PCI or rescue PCI (86.1% *vs.* 89.6%, p=0.003).

Patients with and without prior CVD had substantial differences in their clinical profile. Patients with CVD were older (mean age 66.8±12.8 *vs.* 63.0±12.9 years, p <0.001), and they were more frequently men than those without prior CVD (83% *vs.* 77%, p=0.003). Moreover, they had more comorbidities such as hypertension (71.8% *vs.* 46.8%, p<0.001), diabetes (40.2% *vs.* 22.3%, p<0.001), and dyslipidaemia (70.6% *vs*. 40.4%, p<0.001), compared to patients without CVD. Patients without prior CVD presented with higher percentage of Killip class I (83% *vs.* 73.6%, p<0.001), and longer pain to balloon delays (200 [138-336] *vs.* 189 [128-305] minutes, p=0.011).

Previous CVD, sex and 30-day mortality

There were 337 (8.1%) deaths at 30-day follow up. The crude 30-day mortality was higher for women compared to men (10.4 *vs.*7.4%, p=0.003), whereas it was also higher in those with prior CVD with respect to those without CVD (13.7% *vs.*6.8%, p <0.001).

In the univariate logistic regression model, the odds for dying withing 30 days were 45% higher in women than in men (OR=1.45, 95% CI=1.13-1.86, p=0.003), whereas the odds of having the outcome within 30 days was 117% higher given previous CVD compared to lack of previous CVD (OR=2.17, 95%CI=1.67-2.80, p<0.001). In the multivariate logistic regression model, neither sex nor previous CVD were significantly associated with 30-day mortality (**Figure 1**).

Sex and 30-day mortality by previous CVD status

A stratified analysis of crude 30-day mortality by sex and the presence of prior CVD status is shown in **Figure 2 (panel A).** Among patients without CVD, women had a higher risk to die within 30 days compared to men (10.0% *vs.*5.9%, p<0.001), while among those with CVD there was no significant difference in terms of mortality between women and men (11.0% *vs.*14.3%, p=0.345). From a different angle, the same data showed that mortality was similar in women with and without CVD (11.0% *vs.*10.0%, p=0.737), but was very different in men with and without CVD (14.3% *vs.*5.9%, p<0.001). Key differential characteristics of patients with and without CVD by sex are displayed in Supplementary **Table S2**.

Index event bias introduced by conditioning on CVD status

In an exercise aimed to illustrate a potential index event bias, the association between sex and mortality was evaluated in a selected population (patients with CVD) and compared to the unselected population of patients with and without CVD (i.e., the original cohort with and without CVD).

Whereas in the unselected population there was not an association between women and mortality after adjusting for confounding (OR 1.08, 95% CI=0.75-1.55, p=0.691), this

association was reversed in the selected cohort of patients with previous CVD (OR 0.25, 95% CI= 0.09-0.70, p=0.008) (**Table S3**). As a result of selecting patients based on the presence of CVD, female sex became a "protective" risk factor, when in fact there was no association in the unselected population.

Whereas statistical differences between women and men were mostly consistent in the unselected and selected cohorts (**Table S4**), the big difference between both cohorts was the overall prevalence of cardiovascular risk factors – patients with CVD had a higher prevalence compared to those without CVD (**Table 2**). Because these risk factors have congruent effects on the index and recurrent events, conditioning on having CVD induces dependence between risk factors, tending to bias the association between women and mortality (index event bias). Similarly, age and diabetes were not significantly associated with the outcome in the selected cohort with CVD (OR 1.32, 95% CI=0.94-1.84, p=0.105; and OR 1.53, 95% CI=0.72-3.26, p=0.272, respectively), while they were indeed risk factors of 30-day mortality in the unselected population (**Figure 1**).

Previous CVD and sex interaction

After evaluating stratified models, we tested whether there was a significant interaction between sex and CVD in the multivariate regression model (Supplementary **Table S5**). The multivariate model including the interaction showed that the risk of dying within 30 days was lower in women compared to men for those with CVD (OR=0.30, 95% CI=0.12-0.80), whereas it was similar between women and men among those without CVD (OR=1.17, 95% CI =0.79-1.74; p-for-interaction=0.006). Differences in ORs between the model with and without the interaction are reported in **Figure 2 (panel B)**. The results of the interaction and multivariate logistic regression model with multiple imputation were consistent and are provided in Supplementary **Table S6**.

DISCUSSION

The main findings of this study are: (i) women and patients with previous CVD had a higher crude 30-day mortality risk after STEMI; (ii) after adjustment for confounding, neither sex nor prior CVD were independently associated with short-term mortality; (iii) in a selected cohort of patients with previous CVD, female sex would become a "protective" factor (an illustration of the index event bias); and (iv) there was an interaction between sex and prior CVD (compared to men, the risk of dying within 30 days was lower in women in the subgroup of patients with CVD , whereas it was similar in the subset of patients without CVD).

Mortality in STEMI patients was consistent with the results of previous studies[20,21], with women having persistently higher 30-day crude mortality compared to men[4–6]. Furthermore, female sex has been suggested to be an independent prognostic factor after adjusting for baseline characteristics[5,22–25]. Differences between women and men in short-term mortality in our STEMI cohort may largely be attributed to a less favourable clinical profile, and less guideline-reperfusion treatments, rather than to female-intrinsic factors. Nevertheless, our findings showed that sex was apparently not significantly associated with 30-day mortality after adjusting for potential confounding, in accordance with other studies[4,21,26–28]. There are plenty of studies evaluating the influence of sex on mortality, and some of them have reported discrepant findings. Hence, women have been described to be at higher risk to die after STEMI in younger populations[23–25], or in populations with a higher prevalence of diabetes (45%)[22], in comparison to our cohort (25%). Of note, diabetes is a risk factor with a greater impact on death in women in comparison to men[29]. Notably, there was little evidence about the impact of both sex and the presence of previous CVD, evaluated together for a potential interaction[24].

Data from large, representative registries have demonstrated that around 20% of AMI patients have had a prior AMI[11,30] and that those patients have poor long-term clinical outcomes[9,10,31]. However, the short-term evaluation of clinical outcomes has drawn different findings. Many studies have found little difference in the risk of in-hospital mortality between those with and without previous AMI after adjusting for potential confounding[11–13,30]. Our results were consistent with previous findings in this regard. However, our study has the additive value of showing a significant interaction between sex and prior CVD status (i.e., prior CVD was indeed associated with a lower mortality risk in women following STEMI, compared to men). The lack of poor prognosis among women with CVD compared to men might be explained by a lower coronary burden (previous AMI 53.7% vs 68.4%), and a lower use of evidence-based therapies [8], such as PCI (55.9% vs 68.2%). In line with our findings, Walli-Attaei *et al.*[32] studied differences in CVD in >200 000 patients in the Prospective Urban Rural Epidemiological (PURE) study, showing that women with previous CVD had a lower INTERHEART and Framingham risk scores compared to men with previous CVD. Furthermore, that study revealed that women with a history of CVD had a lower risk of recurrent major CVD events. In addition, our data allow for some speculation about why women have a similar risk than men in the subset of patients without CVD. Compared to men, women without CVD may be at higher risk due to a different distribution of risk factors (hypertension, 54.8% vs 44.5%; smoking, 32.5% vs 50.7%), longer reperfusion times (pain to balloon time >300 min, 32.8% vs. 27.4%), higher Killip class >1 at arrival (20.3% vs 15.7%), or because they received less often reperfusion therapy (84.9% vs 87.6%). In contrast, these differences are attenuated in the subset of patients with CVD, where women and men have a more homogenous clinical profile. Overall, our findings emphasise that a history of CVD does have an impact on short-term prognosis in STEMI patients, although this impact is not the same in women and men.

In the present study, we used the association between sex and CVD as a paradigmatic example of the “index event” bias, illustrating this by selecting only patients with prior CVD.

Because of the congruence between risk factors for the index and recurrent events, the index event bias appeared in several ways. It biased some associations towards the null in the selected cohort, such as age and diabetes, which were actually risk factors in the unselected population. Hence, the prognostic value of age and diabetes is underestimated when conditioning the association on the presence of CVD. Moreover, the index event bias is able to reverse some associations – sex was not associated with mortality in the unselected population but became a "protective" factor in the selected cohort. In STEMI registries, because the index and recurrent events have common risk factors, many so-called paradoxes should be expected, since they are artificially induced by conditioning the analyses on the occurrence of the index event. Of note, the exercise of proving a potential index event bias was aimed to emphasise the need to distinguish between association and causation, which is particularly dangerous in recurrence risk research.

Beyond statistical enlightenments, the complex interplay between sex and prior CVD in short-term mortality needs some further attention. Our findings have relevant clinical implications. Women without previous CVD should receive the same medical management than those with previous CVD – one of the questions that arises is why the difference in mortality between women and men is not consistent across subgroups. It is unclear whether this can be explained by biological differences, or by an unbalance in treatment management. Perhaps women are treated differently than men in the index event, but similarly to them in the recurrent event. CVD might arise awareness about severity regardless of sex. This would justify why the risk ratio varies across subgroups and is not consistently favouring women in both subgroups[8]. In any case, the underlying reasons for the interaction should be addressed in further studies adequately powered to evaluate differences in clinical profile and medical management. Understanding these may lead to better stratify risk in STEMI patients, and to evaluate whether some subsets of patients might benefit the most from intensifying secondary prevention measures. Finally, the identification of an interaction might have statistical

implications for randomised clinical trials, where the expected number of events in the control group is a key feature to estimate the sample size.

LIMITATIONS

This study used prospective data from a nationwide representative cohort of patients with STEMI. Our findings should be evaluated in the light of its own limitations. Given the observational nature of our study, we cannot rule out any residual confounding, although we were able to adjust for a wide range of clinical characteristics. There was no data about previous peripheral disease, or post-AMI medications. The association of prior CVD and sex with 30-day mortality cannot be interpreted as a causal relationship, and caution should be exercised when extrapolating these findings to other populations (e.g., younger cohorts with different prevalence of comorbidities). Given the large magnitude of the association, the statistical power was enough to detect interactions despite the low number of events in the subgroup of women without CVD. The likelihood of having a type I error in our interaction test is relatively small, given that this type of analysis is more likely to incur in type II errors because of problems with sample size[33]. Nevertheless, we might lack statistical power to detect some differences in the stratified analysis (e.g., there were 670 patients with prior CVD, and the number of events for men and women were 79 and 13, respectively). Some of the conclusions drawn in this study might not be generalisable in the current scenario of a global pandemic[34].

CONCLUSIONS

Using a large nationwide contemporary representative cohort of patients with STEMI, we found a different 30-day mortality risk between women and men based on the presence of previous CVD. Compared to men, women had a similar prognosis in the subset of patients without CVD, whereas they were associated with a lower risk of mortality among those with prior CVD. When analyses are conditioned to selected populations (e.g., those with previous

CVD), the association between some risk factors and mortality might be blunted (e.g., age and diabetes), or even reversed (e.g., sex female). Further research is needed to understand why women have a similar mortality risk than men in the subgroup of patients without CVD, whilst they have an actual lower risk in the subset of participants with CVD.

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APPENDIX

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FIGURE LEGENDS

Figure 1. Adjusted multivariate logistic regression model for 30-day mortality.

CVD: Cardiovascular disease; STEMI: ST-elevation myocardial infarction.

Figure 2. Association between 30-day mortality and sex by prior CVD status

Panel A shows crude 30-day all-cause mortality by sex, according to prior CVD status (univariate stratified analysis). **Panel B** shows a forest plot with adjusted ORs for 30-day mortality in multivariate models with and without the interaction term (*sex x prior CVD*). Risk of 30-day mortality is expressed as odds ratio with its 95% CI after adjustment for potential confounding.

CVD: Cardiovascular disease.

TABLES

Table 1. Characteristics of STEMI patients according to sex

Variables	Overall (n=4366)	Women(n=962)	Men (n=3403)	p-value
Age, years	63.7±13	69.5±13.3	62.0±12.4	<0.001
Clinical history				
Hypertension	2210(51.0)	550(57.9)	1659(49)	<0.001
Current Smoker	1895(44.4)	291(30.8)	1604(48.3)	<0.001
Diabetes mellitus	1091(25.3)	250(26.4)	841(25.0)	0.365
Dyslipidaemia	1961(45.3)	441(46.6)	1519(45.0)	0.364
Previous MI	452(10.5)	65(6.9)	387(11.5)	<0.001
Previous PCI	445(10.5)	66(7.1)	379(11.5)	<0.001
Previous CABG	51(1.2)	11(1.2)	40(1.2)	0.956
Prior revascularization without MI	102(2.5)	17(1.9)	85(2.6)	0.181
Previous stroke	176(4.2)	48(5.2)	128(3.9)	0.079
First medical contact				0.666
Emergency medical service or primary care centre,	2469(59.5)	555(58.7)	2002(59.6)	
Non-Primary PCI centre	925(22.3)	209(22.1)	755(22.5)	
Primary PCI centre	759(18.3)	181(19.2)	600(17.9)	
Anterior MI	1796(45.6)	394(44.4)	1469(46)	0.414
Killip class				0.001
I	3346(81.7)	727(77.8)	2734(82.5)	
II- IV	751(18.3)	207(22.2)	579(17.5)	
Pain to balloon time, minutes	197(135-330)	214(141-368)	195(135-320)	0.039
Pain to balloon time				0.007
<150 min	1246(32.4)	244(29.8)	1002(33.2)	
150-300 min	1513(39.4)	310(37.8)	1203(39.8)	
>300 min	1082(28.2)	266(32.4)	815(27.0)	
First Treatment Decision				0.028
Fibrinolysis	173(3.9)	25(2.6)	147(4.3)	
Primary PCI	3854(88.3)	853(88.7)	3001(88.2)	
Transfer to hospital	339(7.8)	84(8.7)	255(7.5)	
Radial access	3732(89.9)	790(86.5)	2942(90.9)	<0.001
Coronary artery disease				0.028
0 vessel disease	203(4.7)	58(6.0)	145(4.3)	
1-vessel disease	2586(59.4)	587(61.1)	1999(58.9)	
2-vessel disease	952(21.9)	195(20.3)	756 (22.3)	
3-vessel disease or left main	623(14.1)	120(12.5)	492(14.5)	
Location of culprit vessel				
Left main coronary artery	69(1.6)	10 (1.0)	59 (1.7)	0.131
Left anterior descending	1795(41.1)	384 (39.9)	1,411 (41.5)	0.393
Left circumflex	643(14.7)	137(14.2)	506(14.9)	0.627
Right coronary artery	1578(36.1)	356(37.0)	1221(35.9)	0.521
Bypass graft	17(0.4)	2(0.2)	15(0.4)	0.306
Initial TIMI flow 0/1	3208(77.7)	697(77.4)	2511(77.8)	0.839
Decision after coronariography				0.001
Primary PCI	3767(86.4)	817(84.9)	2950(86.8)	
Rescue PCI	104(2.4)	11(1.1)	93(2.7)	
Routine early PCI after fibrinolysis	72(1.7)	16(1.7)	55(1.6)	
No reperfusion	216(5.0)	60(6.2)	156(4.6)	
No significant coronary disease	202(4.6)	58(6.0)	144(4.2)	
30-day all-cause mortality	337(8.1)	96(10.4)	241(7.4)	0.003

Data are number (%), mean (SD) or median (IQR). MI: myocardial infarction. PCI: percutaneous coronary intervention. CABG: coronary artery bypass grafting.

Table 2. Characteristics of STEMI patients according to the presence or absence of previous CVD

Variables	Overall (n=4366)	No Previous CVD (n=3517)	Previous CVD (n=691)	p-value
Age, years	63.7±13	63.0±12.9	66.8±12.8	<0.001
Men	3403(78)	2721(77.4)	570(82.5)	0.003
Clinical history				
Hypertension	2210(51.0)	1645(46.8)	495(71.8)	<0.001
Current Smoker,	1895(44.4)	1614(46.5)	216(32.5)	<0.001
Diabetes mellitus	1091(25.3)	781(22.3)	274(40.2)	<0.001
Dyslipidaemia	1961(45.3)	1417(40.4)	486(70.6)	<0.001
First medical contact				0.106
Emergency medical service or primary care centre, n (%)	2469(59.5)	2079(59.9)	390(57.3)	
Non-Primary PCI centre, n (%)	925(22.3)	778(22.4)	147(21.6)	
Primary PCI centre, n (%)	759(18.3)	615(17.7)	144(21.2)	
Anterior MI	1796(45.6)	1503(45.3)	293(47.1)	0.403
Killip class				<0.001
I	3346(81.7)	2853(83.3)	493(73.6)	
II- IV	751(18.3)	574(16.8)	177(26.4)	
Pain to balloon time, minutes	197(135-330)	200(138-336)	189(128-305)	0.011
Pain to balloon time				0.014
<150 min	1246(32.4)	985(31.5)	220(37.7)	
150-300 min	1513(39.4)	1246(39.9)	215(36.8)	
>300 min	1082(28.2)	893(28.6)	149(25.5)	
First Treatment Decision				0.284
Fibrinolysis	173(3.9)	141(4.0)	26(3.8)	
Primary PCI	3854(88.3)	3112(88.5)	601(87)	
Transfer to hospital	339(7.8)	264(7.5)	64(9.3)	
Radial access	3732(89.9)	3057(91.2)	543(83.2)	<0.001
Coronary artery disease				<0.001
0 vessel disease	203(4.7)	154(4.3)	37(4.6)	
1-vessel disease	2586(59.4)	2146(61.1)	357(52.5)	
2-vessel disease	952(21.9)	756(21.5)	155(22.8)	
3-vessel disease or left main	623(14.1)	459(13.1)	131(19.3)	
Location of culprit vessel				
Left main coronary artery	69(1.6)	50(1.4)	16(2.3)	0.084
Left anterior descending	1795(41.1)	1453(41.3)	278(40.2)	0.597
Left circumflex	643(14.7)	538(15.3)	81(11.7)	0.015
Right coronary artery	1578(36.1)	1278(36.3)	248(35.9)	0.823
Bypass graft	17(0.4)	1(0.0)	16(2.3)	<0.001
Initial TIMI flow 0/1	3208(77.7)	2600(78)	502(77)	0.569
Decision after coronariography				0.388
Primary PCI	3767(86.4)	3053(86.9)	585(84.7)	
Rescue PCI	104(2.4)	82(2.3)	16(2.3)	
Routine early PCI after fibrinolysis	72(1.7)	61(1.7)	11(1.6)	
No reperfusion	216(5)	163(4.6)	42(6.1)	
No significant coronary disease	202(4.6)	153(4.4)	37(5.4)	
30-day all-cause mortality	337(8.1)	229(6.8)	92(13.7)	<0.001

Data are number (%), mean (SD) or median (IQR). CABG: coronary artery bypass grafting. CVD: Cardiovascular disease. MI: myocardial infarction. PCI: percutaneous coronary intervention.

Author statement

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