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Sex Differences in 10-Year Outcomes Following STEMI

A Subanalysis From the EXAMINATION-EXTEND Trial

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ABSTRACT

BACKGROUND Short-term outcomes following ST-segment elevation myocardial infarction (STEMI) in women are worse than in men, with a higher mortality rate. It is unknown whether sex plays a role in very long term outcomes.

OBJECTIVES The aim of this study was to assess whether very long term outcomes following STEMI treatment are influenced by sex.

METHODS EXAMINATION-EXTEND (10-Year Follow-Up of the EXAMINATION Trial) was an investigator-driven 10-year follow-up of the EXAMINATION (A Clinical Evaluation of Everolimus Eluting Coronary Stents in the Treatment of Patients With ST-Segment Elevation Myocardial Infarction) trial, which randomly 1:1 assigned 1,498 patients with STEMI to receive either everolimus-eluting stents or bare-metal stents. The present study was a subanalysis according to sex. The primary endpoint was the composite patient-oriented endpoint (all-cause death, any myocardial infarction, or any revascularization) at 10 years. Secondary endpoints were individual components of the primary endpoint. All endpoints were adjusted for age.

RESULTS Among 1,498 patients with STEMI, 254 (17%) were women. Overall, women were older, with more arterial hypertension and less smoking history than men. At 10 years, no difference was observed between women and men for the patient-oriented composite endpoint (40.6% vs 34.2%; adjusted HR: 1.14; 95% CI: 0.91-1.42; $P = 0.259$). There was a trend toward higher all-cause death in women vs men (27.6% vs 19.4%; adjusted HR: 1.30; 95% CI: 0.99-1.71; $P = 0.063$), with no difference in cardiac death or other endpoints.

CONCLUSIONS At very long term follow-up, there were no differences in the combined patient-oriented endpoint between women and men, with a trend toward higher all-cause death in women not driven by cardiac death. The present findings underline the need for focused personalized medicine in women after percutaneous revascularization aimed at both cardiovascular and sex-specific risk factor control and targeted treatment. (10-Years Follow-Up of the EXAMINATION Trial [EXAMINAT10N]; NCT04462315) (J Am Coll Cardiol Intv 2022;15:1965-1973)

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ABBREVIATIONS AND ACRONYMS

BMI = body mass index

BMS = bare-metal stent(s)

CAD = coronary artery disease

DES = drug eluting stent(s)

MI = myocardial infarction

PCI = percutaneous coronary intervention

POCE = patient-oriented composite endpoint

STEMI = ST-segment elevation myocardial infarction

TLR = target-lesion revascularization

TV-MI = target-vessel MI

TVR = target vessel revascularization

Coronary artery disease (CAD) is the most common cause of death among both men and women. However, there are varying outcomes in men and women with symptomatic CAD. CAD develops on average 10 years later in women than in men,[1,2] and there is some evidence suggesting that women have worse mortality than men. These studies were limited to 5-year follow-up, and they used bare-metal stents (BMS).[3,4] Moreover, over the past decade, mortality has declined more rapidly in men than in women.[5,6]

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Specifically, in a ST-segment elevation myocardial infarction (STEMI) population, it is known that women have higher mortality than men both during hospitalization and after discharge for up to 1 year.[7-9] This worse prognosis may be related to differences in baseline clinical characteristics, with women having a worse cardiovascular risk profile.[10] Moreover, women are less likely than men to receive standard-of-care therapies, such as invasive coronary angiography and reperfusion after acute coronary syndromes.[11] On top of this, there is a lack of data concerning the impact of sex on very long term outcomes beyond 1 year.

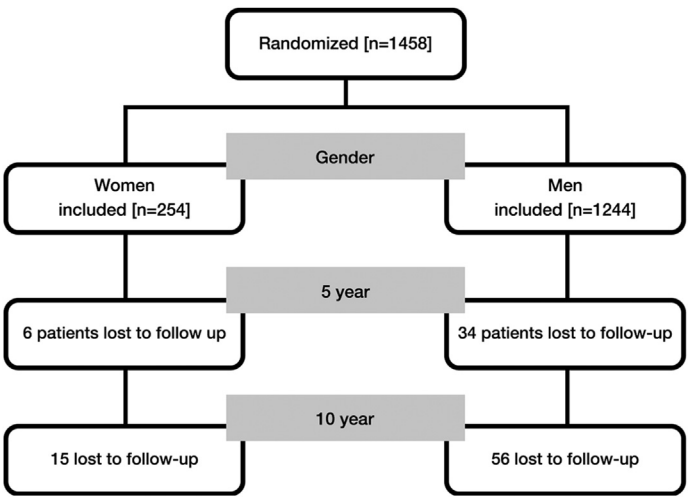
The aim of this study was to analyze the impact of sex on 10-year outcomes of patients with STEMI treated using primary percutaneous coronary intervention (PCI) included in EXAMINATION-EXTEND (10-Year Follow-Up of the EXAMINATION Trial).

METHODS

STUDY DESIGN AND PATIENTS. The EXAMINATION (A Clinical Evaluation of Everolimus Eluting Coronary Stents in the Treatment of Patients With ST-Segment Elevation Myocardial Infarction) trial (NCT00828087) was an all-comers, multicenter, prospective, 1:1 randomized, 2-arm, single-blind, controlled trial conducted at 12 centers in 3 countries, with the aim of assessing the superiority of an everolimus-eluting stent (XIENCE V, Abbott Vascular) vs a BMS (Multilink Vision, Abbott Vascular) in patients with STEMI for the primary endpoint of all-cause death, any myocardial infarction, and any revascularization at 1 year. The study had broad inclusion criteria and few exclusion criteria to ensure an all-comers STEMI population representative of routine clinical practice. Outcomes of the study have been reported up to the fifth year.[12,13] Once it completed 5 years of follow-up, EXAMINATION was reinitiated as the EXAMINATION-EXTEND study to evaluate the patient-oriented composite endpoint (POCE) and device-oriented composite endpoint at 10 years. The EXAMINATION-EXTEND study is registered at ClinicalTrials.gov (NCT04462315) as an investigator-driven extension of follow-up of the EXAMINATION trial. Medical ethics committee approval for this study was granted at the institutions of the principal investigators (Hospital Clinic and Hospital Bellvitge, Barcelona, Spain). The requirement to obtain informed consent to gather information on 10-year events was waived, and follow-up was performed in accordance with local law and the regulations of each participating site and complied with the Declaration of Helsinki.

Independent study monitors (ADKNOMA) verified the adequacy of the extended follow-up and events reported. All events were adjudicated and classified by an independent event adjudication committee blinded to the treatment groups (Barcicore Lab). The 10-year primary endpoint results of the

FIGURE 1 Flowchart of the Study Up to 10-Year Follow-Up



A total of 1,498 patients were initially recruited. At 10 years, clinical follow-up was obtained in 95.2% of the patients.

The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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EXAMINATION-EXTEND study have been published previously.[14]

For the purpose of this analysis, the primary and secondary outcomes have been stratified according to sex.

STUDY ENDPOINTS. The primary endpoint of this study was the POCE of all-cause death, any myocardial infarction, or any revascularization at 10 years. Secondary endpoints were the individual components of the primary endpoint, cardiac death, target vessel myocardial infarction, target lesion revascularization, and stent thrombosis.[15,16] Detailed descriptions of the study endpoints and definitions have been published previously.[15,16]

STATISTICAL ANALYSIS. Categorical variables are presented as absolute and relative frequencies and continuous variables as mean ± SD (or median with IQR as appropriate).

Clinical variables at 1, 5, and 10 years are presented as incidence (95% CI) and were compared using the chi-square or Fisher exact test. For time-to-event variables, survival curves were constructed by sex using Kaplan-Meier estimates and log-rank test results. In addition, HRs (with 95% CIs) and *P* values calculated from Cox proportional hazards models were adjusted for age. Landmark analyses were performed from 0 to 5 years and from 5 to 10 years of follow-up to assess the effect of time on the occurrence of events.

Two-tailed *P* values <0.05 were considered to indicate statistical significance. SAS version 9.4 (SAS Institute) was used for all analyses.

TABLE 1 Baseline Characteristics of Patients by Sex

	Male (n = 1,244)	Female (n = 254)	*P* Value
Age, y	59.83 ± 11.98	67.93 ± 12.21	0.001
Body mass index, kg/m^2	27.4 ± 3.5	27.0 ± 5.0	0.126
Coronary risk factors			
(Previous) smoking	989 (79.5)	93 (36.6)	0.001
Diabetes mellitus	212 (17.0)	46 (18.1)	0.681
Arterial hypertension	567 (45.6)	158 (62.2)	0.001
Hyperlipidemia	534 (42.9)	121 (47.6)	0.168
Family history	211 (17.0)	42 (16.5)	0.869
Cardiovascular history			
Previous myocardial infarction	68 (5.5)	12 (4.7)	0.632
Previous PCI	52 (4.2)	9 (3.5)	0.639
Previous CABG	10 (0.8)	0 (0.0)	0.152
Previous stroke	22 (1.8)	9 (3.5)	0.070
Clinical condition			0.663
Primary PCI (<12 h)	1,050 (84.4)	218 (85.8)	
Rescue PCI	86 (6.9)	12 (4.7)	
PCI after successful thrombolysis	29 (2.3)	5 (2.0)	
Latecomer (>12 and <48 h)	78 (6.3)	19 (7.5)	
Clinical status on admission			0.064
Killip class I	1,118 (89.9)	219 (86.2)	
Killip class II	95 (7.6)	20 (7.9)	
Killip class III	15 (1.2)	8 (3.1)	
Killip class IV	13 (1.0)	5 (2.0)	
Infarct-related artery			0.108
Left anterior descending coronary artery	510 (41.6)	118 (47.7)	
Left circumflex coronary artery	183 (14.2)	26 (11.0)	
Right coronary artery	543 (43.4)	108 (40.1)	
Left main coronary artery	3 (0.3)	0 (0.0)	
Saphenous vein graft	5 (0.5)	2 (1.2)	
Multivessel disease	157 (12.6)	31 (12.2)	0.855
Ejection fraction, %[a]	51.1 ± 10.3	50.9 11.3	0.895

Values are mean ± SD or n (%). [a]Ejection fraction was calculated in 884 men (71.1%) and in 172 women (67.7%).
CABG = coronary artery bypass graft; PCI = percutaneous coronary intervention.

RESULTS

PATIENT CHARACTERISTICS. Of the 1,498 patients randomized, a total of 254 patients (17.0%) were women and 1,244 (83%) were men (**Figure 1**).

Baseline demographic and clinical characteristics of all patients are shown in **Table 1**. Overall, women were older, with fewer smokers and a higher prevalence of hypertension than among men. Both groups were similar regarding procedural data, except for lower use of manual thrombectomy and glycoprotein IIb/IIIa inhibitors in women compared with men. Procedural characteristics by sex are shown in **Table 2**.

The median duration of follow-up was 10.0 years (IQR: 9.56-10.0 years).

10-YEAR OUTCOMES. At 10-year follow-up, the POCE had occurred in 103 women (40.6%) and in 426 men (34.2%) (adjusted HR: 1.14; 95% CI: 0.91-1.42; *P* = 0.259) (**Table 3, Figure 2**). A trend toward higher all-cause death was observed in women, occurring in 70 women (27.6%) and 249 men (19.4%) (adjusted HR: 1.30; 95% CI: 0.99-1.71; *P* = 0.063). The rate of cardiac death did not differ between groups (adjusted HR: 1.19; 95% CI: 0.82-1.72; *P* = 0.356). No differences were found in terms of other secondary endpoints between the 2 groups (**Table 3, Central Illustration**).

LANDMARK ANALYSES. With respect to the primary POCE, no difference was observed in the landmark analysis either between 0 and 5 years or between 5 and 10 years of follow-up. Also, no differences were found for all-cause, cardiac death, or myocardial infarction (**Figure 3**). Regarding all revascularization, a higher rate was observed in men than in women within the first 5 years of follow-up but not in the subsequent 5 years (**Figure 3,** Supplemental Table A).

10-YEAR POCE PREDICTORS IN MEN AND WOMEN. In women, on univariate analysis, age, arterial hypertension, and multivessel disease were significantly associated with POCE; on multivariate analysis,

TABLE 2 Periprocedural Characteristics by Sex

	Male (n = 1,244)	Female (n = 254)	Difference (95% CI)[a]	*P* Value[b]
TIMI flow grade before PCI				0.546[c]
0	727 (58.4)	160 (63.0)	−4.6 (−11.1 to 2.0)	
1	99 (8.0)	16 (6.3)	1.7 (−1.7 to 5.0)	
2	169 (13.6)	30 (11.8)	1.8 (−2.6 to 6.2)	
3	249 (20.0)	48 (18.9)	1.1 (−4.2 to 6.4)	
Anticoagulation regimen				
Unfractionated heparin	992 (79.7)	197 (77.6)	2.2 (−3.4 to 7.8)	0.433
Low-molecular weight heparin	111 (8.9)	22 (8.7)	0.3 (−3.5 to 4.1)	0.893
Bivalirudin	86 (6.9)	19 (7.5)	−0.6 (−4.1 to 3.0)	0.747
Antiplatelet regimen				
Aspirin before PCI	1,161 (93.3)	227 (89.4)	4.0 (0.0 to 8.0)	0.027
Clopidogrel before PCI	1,179 (94.8)	239 (94.1)	0.7 (−2.5 to 3.8)	0.660
Glycoprotein IIb/IIIa inhibitor	671 (53.9)	114 (44.9)	9.1 (2.3 to 15.8)	0.008
Manual thrombectomy	826 (66.4)	150 (59.1)	7.3 (0.8 to 13.9)	0.025
Type of stent				0.155
EES/DES	634 (51.0)	117 (46.1)	4.9 (−1.8 to 11.6)	
Multilink Vision/BMS	610 (49.0)	137 (53.9)	−4.9 (−11.6 to 1.8)	
Direct stenting	746 (60.0)	139 (54.7)	5.2 (−1.5 to 11.9)	0.121
Postdilatation	187 (15.0)	34 (13.4)	1.6 (−3.0 to 6.3)	0.500
Overlapping stent	333 (26.8)	71 (28.0)	−1.2 (−7.2 to 4.9)	0.698
Number of stents	1.39 ± 0.7	1.37 ± 0.6	0.02 (−0.07 to 0.11)[d]	0.671[d]
Total stent length, mm	23.0 (18.0 to 35.0)	23.0 (18.0 to 33.0)	0.00 (0.00 to 0.00)	0.387[e]
TIMI flow grade after PCI				0.508[c]
0	19 (1.5)	7 (2.8)	−1.2 (−3.4 to 0.9)	
1	10 (0.8)	2 (0.8)	0.0 (−1.2 to 1.2)	
2	51 (4.1)	8 (3.2)	1.0 (−1.5 to 3.4)	
3	1,160 (93.5)	236 (93.3)	0.3 (−3.1 to 3.8)	

Values are n (%), mean ± SD, or median (IQR). [a]Normality assumed. [b]Two-sided Fisher exact test. [c]Cochran-Mantel-Haenszel test. [d]Student's *t*-test. [e]Median 2-sample test.

BMS = bare-metal stent(s); DES = drug-eluting stent(s); EES = everolimus-eluting stent(s); PCI = percutaneous coronary intervention; TIMI = Thrombolysis In Myocardial Infarction.

TABLE 3 Clinical Events up to 10 Years by Sex

	Male (n = 1,244)	Female (n = 254)	*P* Value	Adjusted HR[a] (95% CI)	*P* Value[a]
Patient-oriented composite endpoint[b]	426 (34.2)	103 (40.6)	0.071	1.14 (0.91-1.42)	0.259
All-cause death[c]	241 (19.4)	70 (27.6)	0.002	1.30 (0.99-1.71)	0.063
Cardiac	126 (10.1)	40 (15.7)	0.007	1.19 (0.82-1.72)	0.356
Any myocardial infarction[d]	70 (5.6)	15 (5.9)	0.833	0.78 (0.44-1.39)	0.405
Target vessel related	41 (3.3)	11 (4.3)	0.394	0.64 (0.32-1.27)	0.201
Non-target vessel related	29 (2.3)	5 (2.0)	0.719	0.96 (0.37-2.57)	0.948
Any revascularization	233 (18.7)	36 (14.2)	0.087	1.26 (0.88-1.82)	0.197
Target lesion	95 (7.6)	12 (4.7)	0.104	1.43 (0.77-2.65)	0.249
Target vessel	145 (11.7)	19 (7.5)	0.053	1.43 (0.88-2.34)	0.148
Non-target vessel	88 (7.1)	17 (6.7)	0.818	1.05 (0.61-1.79)	0.856
Definite stent thrombosis[e]	32 (2.6)	3 (1.2)	0.180	1.84 (0.55-6.14)	0.319
Definite/probable stent thrombosis[e]	38 (3.1)	7 (2.8)	0.802	1.08 (0.47-2.48)	0.850

Values are n (%). [a]Cox regression adjusting for age. [b]Combined endpoint of all-cause death, any recurrent myocardial infarction, and any revascularization. [c]Death was adjudicated according to the Academic Research Consortium definition. [d]Myocardial infarction was adjudicated according to the World Health Organization extended definition. [e]Stent thrombosis was defined according to the Academic Research Consortium definition.

only age (HR: 1.06; 95% CI: 1.04-1.09; $P < 0.001$) and arterial hypertension (HR: 1.93; 95% CI: 1.07-3.51: $P = 0.030$) were independent predictors of POCE.

On the contrary, in men, age, diabetes, arterial hypertension, previous MI, previous PCI and coronary artery bypass graft surgery, previous stroke, multivessel disease, ejection fraction at discharge, and use of BMS were significantly associated with POCE. However, on multivariate analysis, only age (HR: 1.04; 95% CI: 1.03-1.06; $P < 0.001$) and BMS (HR: 1.29; 95% CI: 1.01-1.65; $P = 0.042$) were independent predictors of POCE.

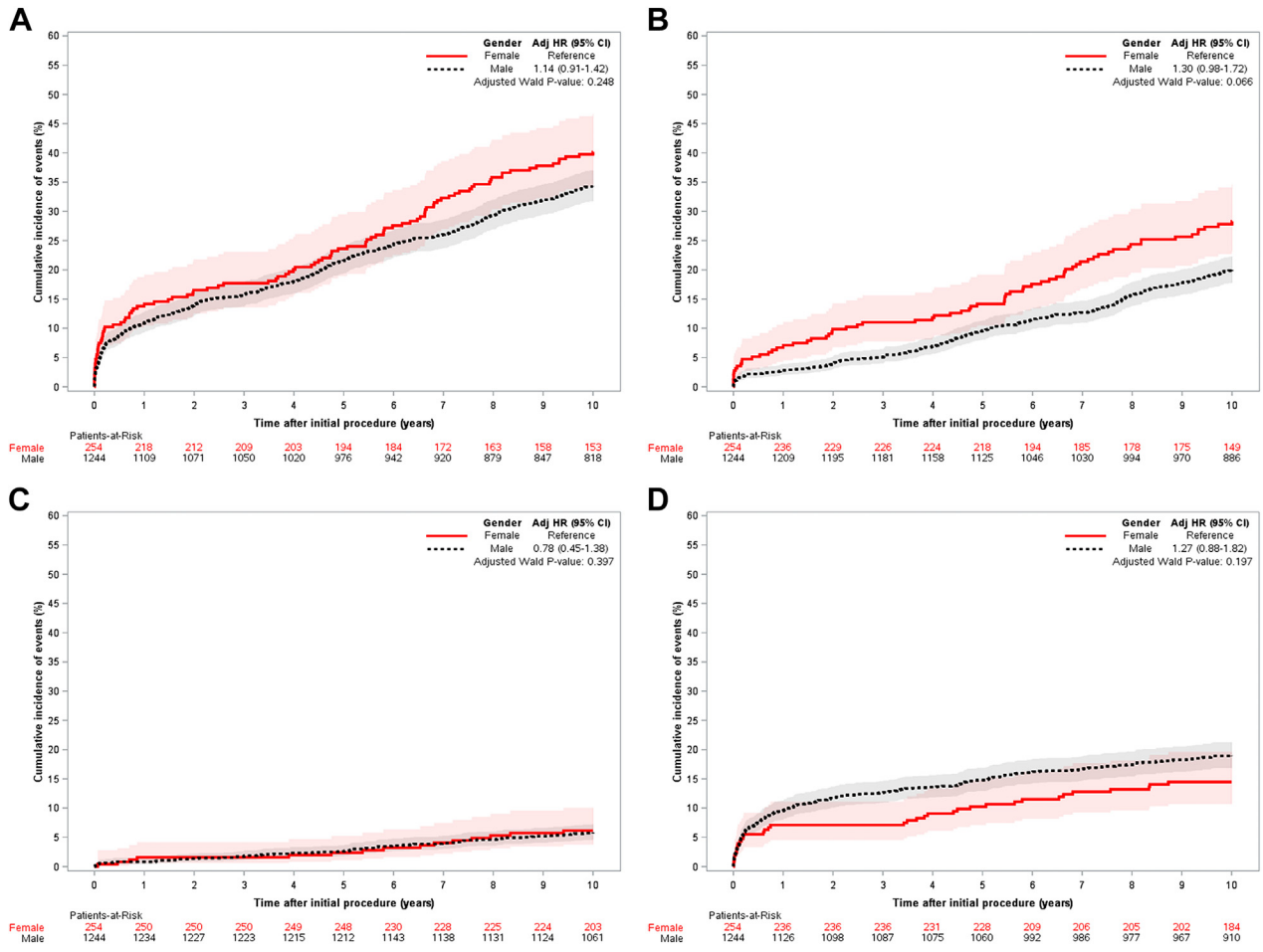
DISCUSSION

This study shows that: 1) women with STEMI did not have worse very long term outcomes in terms of POCE compared with men; 2) however, they exhibited a numerically higher incidence of all-cause death, which was not driven by cardiac death; 3) women had a lower risk for target vessel revascularization (TVR) after STEMI than men in the first 5 years of follow-up, but not thereafter; and 4) age was as an independent predictor of POCE in both men and women.

10-YEAR POCE OUTCOMES ACCORDING TO SEX. Prior studies evaluating the impact of sex on PCI-related outcomes have produced contrasting results,[5,8,17-21] contributing to the ongoing debate as to whether CAD management should vary according to sex.[9,21,22] Worse outcomes in women than men may indeed disappear after correction for confounding factors.[21,23,24] Moreover, few studies have examined long-term sex-related outcomes after PCI, which are based largely on registries and observational data[9,23] (Table 4). The EXAMINATION-EXTEND trial, which enrolled patients across a specific CAD presentation, STEMI, and with more than 95% of the study population being followed up to the 10-year point,[14] offers a unique opportunity for a comprehensive assessment of long-term risks associated with sex. Of note, the number of women enrolled in the trial (n = 254 [17%]) sheds light on the underrepresentation of women in clinical studies. This low percentage is in line with real-world data from the Spanish CODI-IAM registry, in which only 20% were women.[25]

In our study, women were older and more commonly had arterial hypertension, whereas more men were smokers. Diabetes was equal in both groups. Similarly, sex differences in the baseline cardiovascular profile have been demonstrated in many studies and were related to the greater age dependency of CAD in women compared with men; women generally start developing CAD

FIGURE 2 **10-Year Time-to-Event Curves for the Primary Endpoint and Its Individual Components**



Cumulative 10-year incidence is shown with Kaplan-Meier yearly event rates. **(A)** Patient-oriented composite outcome and its individual components: **(B)** all-cause death, **(C)** any myocardial infarction, and **(D)** any revascularization. Adj = adjusted.

predominantly at postmenopausal age, which is 6 to 10 years later than men.[26,27]

In our study, by extending follow-up to 10 years, we found that the rate of POCE was similar between men and women after STEMI, with curves not diverging over time, either during the first 5 years or between 5 and 10 years of follow-up. This outcome analysis was adjusted for age, which was the most important predictor of events in both men and women; we did not find any difference by also adjusting for other baseline clinical variables (data not shown).

LONG-TERM MORTALITY IN STEMI BETWEEN MEN AND WOMEN. Looking specifically at the individual components of POCE, there was a trend toward higher all-cause death at the 10-year follow-up in women compared with men (27.6% vs 19.4%; $P = 0.063$), which was not driven by cardiac deaths (15.7% vs 10.1%; $P = 0.356$).

Life expectancy of patients after STEMI is closely related to their survival in the first 30 days, with consistent data suggesting sex as an independent predictor of in-hospital and up to 30-day mortality,[23,24] implying that heart failure and cardiogenic shock may lead to worse outcomes in women. At long-term follow-up, the available evidence is contradictory,[9,20-22,28] with some studies showing higher long-term all-cause mortality in women vs men[9,22] and others showing no differences.[20,28] Thus, the debate on whether sex plays a role in long-term mortality is still ongoing (Table 4). Our findings are in line with those of some previous studies, showing an unadjusted higher rate of all-cause death in women vs men after PCI, likely related to age and

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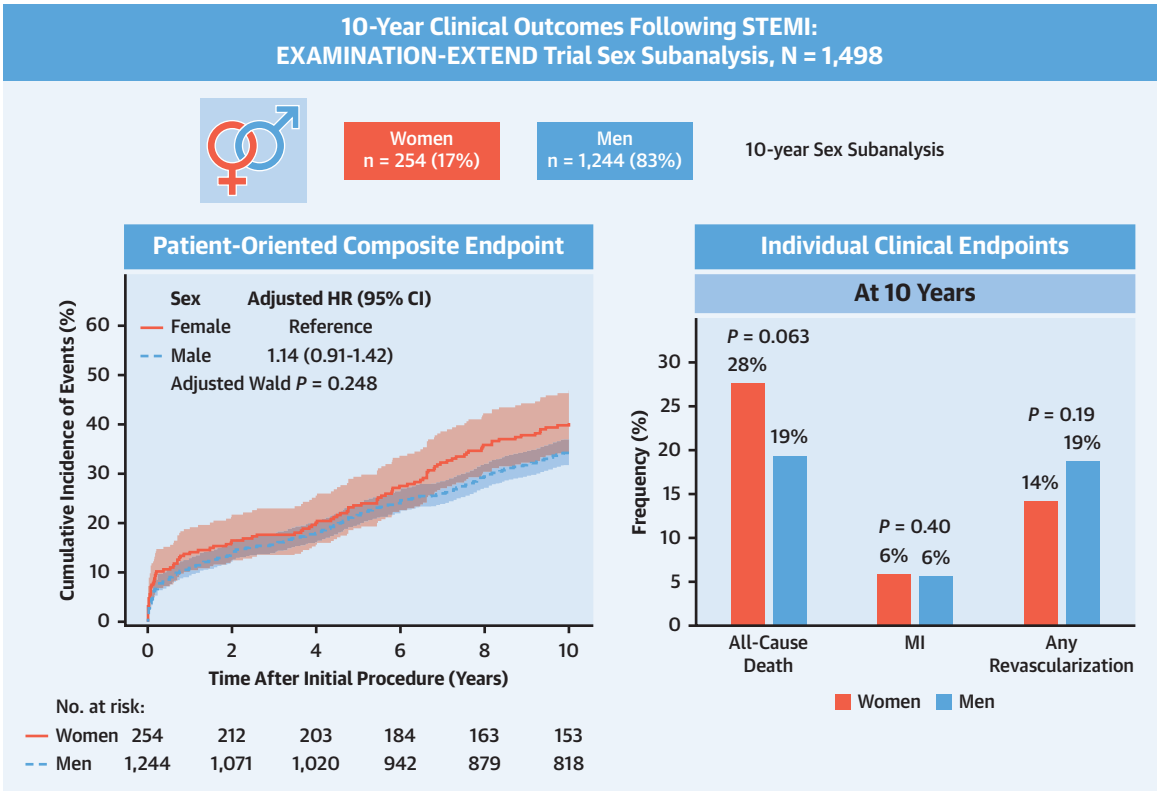
CENTRAL ILLUSTRATION **Outcomes of Patients With ST-Segment Elevation Myocardial Infarction According to Sex at 10-Year Follow-Up**



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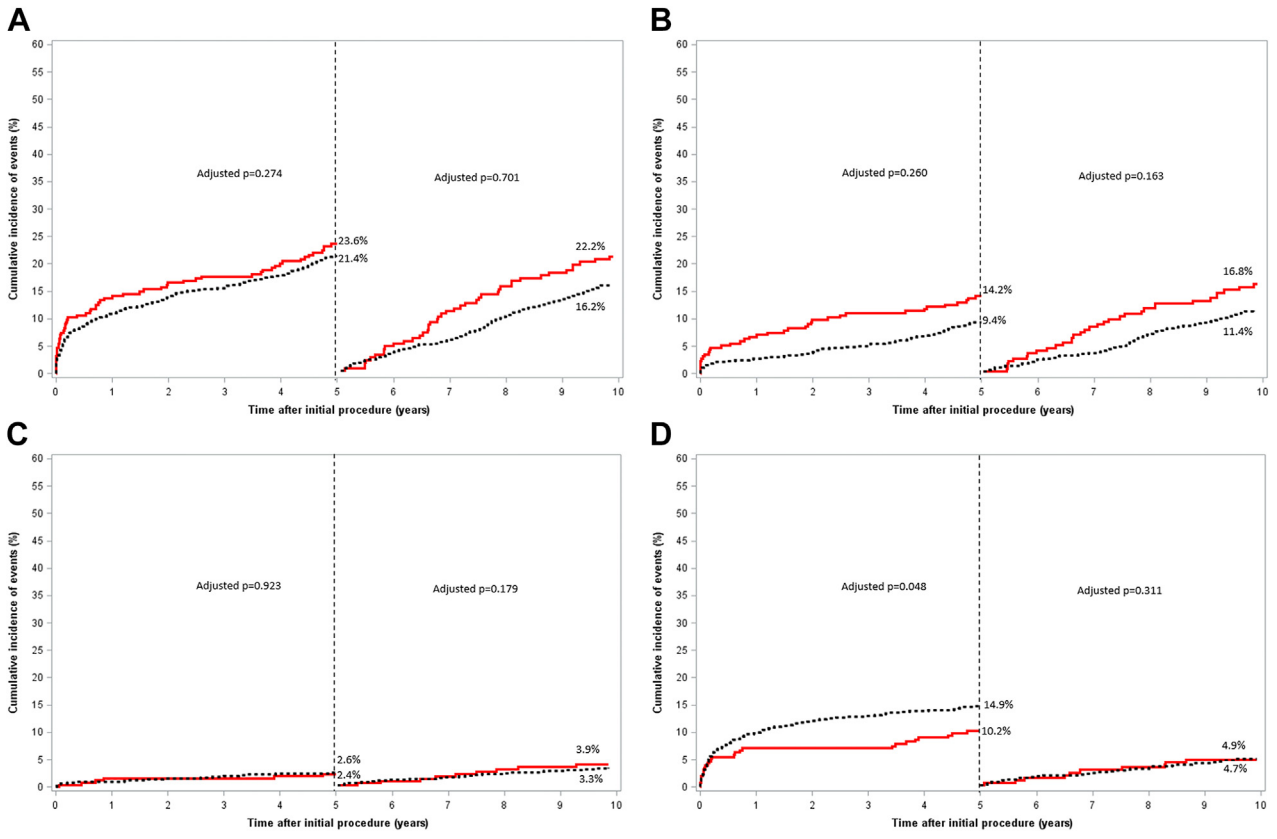
The sex substudy of the EXAMINATION-EXTEND (10-Year Follow-Up of the EXAMINATION Trial) trial demonstrated no statistical differences in the primary patient-oriented composite endpoint between men and women. In addition, at 10-year follow-up, there were no differences in all-cause death, myocardial infarction, or any revascularization.

comorbidities. Specifically, because of the older age at the time of STEMI presentation, more noncardiac comorbidities would have been accumulated, thereby increasing the risk for noncardiac death in the subsequent years. Although further investigation is needed to confirm this finding, we suggest that the focus of prevention should go beyond cardiac death, by managing comorbidities that may be sex associated, in order to prevent noncardiac death. The higher POCE rate in women vs men, related mainly to age and hypertension as the only independent predictors of events, also underlines the need for focused personalized medicine in women after percutaneous revascularization aimed at both cardiovascular and sex-specific risk factor control and targeted treatment. This sex-based attention should be promoted and become the standard of care.

OVER-TIME DISTRIBUTION OF TVR BETWEEN SEXES. Looking at TVR, we noted a different influence of time on this event according to sex. Men had a higher TVR rate than women during the first 5 years of follow-up (9.2% vs 5.1%; $P = 0.042$) but not thereafter (11.7% vs 7.5%; $P = 0.148$). This finding contrasts with existing evidence. A large meta-analysis showed that women had an increased short-term incidence of repeated coronary revascularization compared with men, but with no difference in the long term.[29] This may be related specifically to the expected smaller vessel diameter in women vs men.[24,30] For this reason, a play of chance cannot be excluded.

STUDY LIMITATIONS. Although we undertook careful review of 1 major parent trial to identify all known

FIGURE 3 **Landmark Analysis of Patient-Oriented Outcomes After ST-Segment Elevation Myocardial Infarction**



Landmark analysis from 0 to 5 years and from 5 to 10 years for **(A)** the patient-oriented composite endpoint and its individual components: **(B)** all-cause death, **(C)** any myocardial infarction, and **(D)** any revascularization.

risk factors and therapies provided, we were unable to account for some of the potential variables that may be associated with outcomes or patient management, such as long-term patient adherence to drug treatments.

Our subanalysis included a smaller proportion of women with STEMI than men; thus, our power to assess for differences in outcomes was limited, and our findings should be considered hypothesis generating.

Although age was considered in the multivariate analysis, the 8-year difference in mean age between men and women is unlikely to be reliably corrected by any statistical method, particularly regarding all-cause death. Of note, this age difference was comparable with real-world data from a meta-analysis of 15,000 patients showing a similar difference of 8.5 years between men and women who presented with STEMI. This is most likely because STEMI occurred in women at a later age than in men.[31]

The association between sex and outcomes may be driven by confounders, including over-time lifestyle and behavioral factors, which have not been recorded in the study.

CONCLUSIONS

At 10-year follow-up of patients with STEMI treated with primary PCI, sex was not an influential factor in POCE events. However, there was a trend, albeit nonsignificant, toward higher all-cause death in women compared with men, not explained by cardiac death. Of note also, there was a higher rate of repeat revascularizations in men within the first 5 years of follow-up; this difference leveled out at 10 years, by which time there was no difference.

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TABLE 4 Comparison of Outcomes by Sex in Patients

First Author (Year)	Women	Men	Follow-Up	Endpoint[a]	Results[b]
Regueiro et al (2015)[32]	254 (17.0)	1,244 (83.0)	2 y	Patient-oriented endpoint of all-cause death, any recurrent myocardial infarction, and any revascularization	No differences
Murphy et al (2021)[33]	244 (21.2)	8,336 (78.8)	2.5 y	All-cause mortality	Higher mortality rates in women
Tomassini et al (2020)[34]	484 (24.4)	1,497 (75.6)	30 d and 5 y	All-cause mortality	Higher 30-d mortality in women; no differences at 5 y
Burgess et al (2020)[35]	123 (21.0)	466 (79.0)	30 d, 1 and 3.6 y	Composite of cardiac death or myocardial infarction	Higher rates in composite of cardiac death or myocardial infarction in women at 30 d and 1 and 3.6 y
Stehli et al (2019)[36]	1,317 (20.5)	5,114 (79.5)	30 d	All-cause mortality	Higher mortality rates in women
Fu et al (2018)[23]	227 (11.8)	1,693 (88.2)	30 d, 1 and 3 y	NACE including any bleeding or major adverse cardiac or cerebral events, all-cause death, reinfarction, clinically indicated target vessel revascularization, or stroke	No differences at 30 d and 1 y; higher rates of NACE in women at 3 y
Khan et al (2018)[37]	715 (24.7)	2,183 (75.3)	6 mo	MACE (myocardial reinfarction, stroke, or cardiac death) and all-cause mortality	Higher rates of MACE and all-cause mortality in women
Heer et al (2017)[38]	9,156 (27.8)	23,830 (72.2)	In-hospital	All-cause mortality	Higher mortality rates in women
Biava (2015)[22]	75 (23.1)	250 (76.9)	46.5 mo	All-cause mortality and cardiac death	Higher rate of all-cause mortality and cardiac death in women
de Boer et al (2014)[9]	3,343 (28.0)	8,588 (72.0)	30 d, 1 and 4 y	All-cause mortality	Higher mortality rates in women at 30 d and 1 and 4 y

Values are n (%). [a]Primary endpoints (or secondary when primary endpoint was not related to clinical outcomes). [b]Adjusted results according to baseline characteristics.
MACE = major adverse cardiac event(s); NACE = net adverse clinical event(s).

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PERSPECTIVES

WHAT IS KNOWN? Adverse outcomes after STEMI are suggested to be higher in women than in men in the acute setting and up to 30 days, driven mainly by sex-related pathophysiological differences.

WHAT IS NEW? Very long term outcomes are not influenced by gender but rather by risk factor profile, including age and comorbidities.

WHAT IS NEXT? Focused personalized medicine in women after PCI aimed at both cardiovascular and sex-specific risk factor control and targeted treatment is needed.

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KEY WORDS drug-eluting stent(s), sex, percutaneous coronary intervention, STEMI

APPENDIX For a supplemental table, please see the online version of this paper.