

One-month DAPT after biodegradable-polymer everolimus-eluting stent implantation in women at high-bleeding risk: Insights from the POEM trial

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Abstract

Aims: We conducted a prespecified subanalysis of the POEM trial to assess the association between sex and clinical outcomes following a short 1-month dual-antiplatelet-therapy (DAPT) period after percutaneous coronary intervention (PCI) with bioresorbable polymer everolimus-eluting stent (BP-EES) among patients at high bleeding risk (HBR).

Background: Shortening the DAPT period after PCI is an effective bleeding avoidance strategy with contemporary drug-eluting stents. Whether sex affects the risk of adverse events following PCI is still debated.

Methods: Patients at HBR undergoing PCI with BP-EES were enrolled and treated with 1-month DAPT. If anticoagulation was needed, study participants received an oral anticoagulant (OAC) in addition to a P2Y₁₂ inhibitor for 1 month, followed by OAC only thereafter. The primary endpoint was a composite of cardiac death, myocardial infarction, or definite/probable stent thrombosis at 12 months. We report sex-based outcomes of patients included in the POEM study.

Results: We enrolled 129 (29.1%) women and 314 (70.9%) men. Women were older, with lower hemoglobin levels, and worse renal function. Accordingly, they had a trend for a greater number of HBR criteria fulfilled and a higher PARIS bleeding score. However, they were not at a significantly higher risk for the primary endpoint (men vs. women: 5.17% vs. 3.94%; HR 1.30; 95% CI: 0.48-3.54, $p = 0.61$), or any of the hemorrhagic and ischemic secondary endpoints.

For affiliations refer to page 1137.

Matteo Maurina and Carlo Andrea Pivato contributed equally to this study.

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Conclusions: This prespecified subanalysis of the POEM trial suggests that 1-month DAPT following PCI with BP-EES may be a safe and effective therapeutic strategy for women at HBR.

KEYWORDS

biodegradable polymer, high bleeding risk, percutaneous coronary intervention, sex, short DAPT, women

1 | INTRODUCTION

Reducing the length of dual antiplatelet therapy (DAPT) after percutaneous coronary intervention (PCI) is a frequently adopted bleeding avoidance strategy in patients at high bleeding risk (HBR).^{1–3} However, since both hemorrhagic and thrombotic events impact outcomes following PCI,⁴ this must be done without an excessive increase in ischemic risk. To date, several studies have explored different regimens of short DAPT with contemporary drug-eluting stents (DES) in HBR patients, showing a relatively safe profile of these devices when a short DAPT is pursued.^{5–8}

The POEM (Performance of Bioresorbable Polymer-Coated Everolimus-Eluting Synergy Stent in Patients at HBR Undergoing Percutaneous Coronary Revascularization Followed by 1-Month DAPT) trial showed that a short 1-month DAPT after PCI with the bioresorbable polymer everolimus-eluting stent (BP-EES) is a safe strategy in HBR patients, as it is associated with low rates of ischemic and bleeding events.⁹

The impact of sex as an independent risk factor for adverse events after PCI remains a subject of debate and there is ongoing discordance between guidelines^{10,11} and risk scores^{12–16} regarding whether sex “per se” significantly impacts outcomes. Consequently, the potential benefits of an abbreviated DAPT may not be uniform across sexes. Up to date, only a few studies have explored the impact of sex on outcomes among HBR patients who had undergone PCI with contemporary DES.^{17–19} We conducted a prespecified subanalysis of the POEM trial to assess the impact of sex on clinical outcomes following a short 1-month DAPT after PCI with BP-EES implantation in HBR patients.

2 | METHODS

This study is a prespecified subgroup analysis of the POEM trial, whose design has been previously published.^{9,20,21} In brief, POEM was a noninferiority prospective, single-arm trial conducted at 10 Italian centers from April 2017 to October 2019 (EudraCT Number 2016-004510-99, clinicaltrials.gov NCT03112707).

The 1-year primary endpoint (a composite of cardiac death, myocardial infarction (MI), or definite/probable stent thrombosis at 12-month follow-up) met the noninferiority compared with the predefined objective performance criterion of 9.4% and the

noninferiority margin of 3.85% ($p < 0.001$) notwithstanding the lower-than-expected sample size.

2.1 | Study population

Patients who underwent PCI with a BP-EES were deemed eligible for inclusion if they met at least one of the following criteria: age ≥ 75 years; oral anticoagulation (OAC) therapy; anemia (hemoglobin (Hb) < 11 g/L); transfusion within 4 weeks; thrombocytopenia (platelets $< 100,000$ /mL); bleeding requiring hospitalization within previous 12 months; stroke within previous 12 months; history of intracerebral hemorrhage; severe chronic liver disease; chronic kidney disease (creatinine clearance < 40 mL/min); cancer within the previous 3 years; planned major, noncardiac surgery in the next 12 months; glucocorticoids or nonsteroidal anti-inflammatory drugs planned for > 30 days after PCI; expected nonadherence to DAPT. No clinical or procedural exclusion criteria were defined, except for cardiogenic shock. All participants were treated with 1-month DAPT. In case of need for anticoagulation, patients received OAC in addition to a P2Y₁₂ inhibitor for 1 month followed by OAC alone thereafter.

2.2 | Study endpoints and definitions

The primary endpoint was a composite of cardiac death, MI, or definite or probable stent thrombosis at 12 months. Secondary endpoints included the individual components of the primary endpoint, all-cause death, target-vessel revascularization, target-lesion revascularization (TLR), major bleeding, cerebrovascular events, and target-lesion failure (TLF). An additional secondary endpoint was a patient-oriented composite endpoint (POCE) including the following: all-cause death, any MI, and any revascularization. Standard definitions for outcomes were used: third Universal Definition of Myocardial Infarction for MI,²² Academic Research Consortium (ARC) definitions for stent thrombosis,²³ and Bleeding Academic Research Consortium (BARC) definitions for major bleeding.²⁴ PARIS (patterns of nonadherence to antiplatelet regimen in stented patients) and HAS-BLED (Hypertension, Abnormal Renal/Liver Function, Stroke, Bleeding History or Predisposition, Labile INR, Elderly, Drugs/Alcohol Concomitantly) scores were used to determine bleeding risk at baseline. An independent Clinical Event Committee reviewed and adjudicated events of interest.

2.3 | Statistical analysis

For this prespecified analysis, patients were stratified by sex. All the statistical analyses were performed on the intention-to-treat population. Categorical variables are presented as counts and percentages and were compared using the χ^2 or Fisher's exact test, as appropriate. Continuous variables are expressed as mean and standard deviation or median (interquartile range (IQR)) and were compared using the

Student's *t* or Mann-Whitney U test, as appropriate. Outcomes for the primary and secondary endpoints were analyzed with the time-to-event Kaplan-Meier survival curves and the difference between groups was evaluated with the log-rank test. The composite endpoints were analyzed according to time-to-first event. To assess the association between sex and outcomes, hazard ratios (HRs) and 95% confidence intervals (CIs) were calculated with Cox regression models. A multivariable Cox model was employed to adjust for potential

TABLE 1 Baseline clinical characteristics.

	Men (N = 314)	Women (N = 129)	p-Value
Age, years	73.98 ± 9.05	76.82 ± 9.35	<0.01
BMI, kg/m ²	26.83 ± 3.73	26.19 ± 4.73	0.09
Clinical presentation			0.76
Stable angina	126/313 (40.26)	48/126 (38.10)	
Unstable angina	51/313 (16.29)	16/126 (12.70)	
NSTEMI	54/313 (17.25)	27/126 (21.43)	
STEMI	22/313 (7.03)	10/126 (7.94)	
Evidence of ischemia	60/313 (19.17)	25/126 (19.84)	
Diabetes	120/309 (38.83)	46/127 (36.22)	0.61
Arterial Hypertension	270/311 (86.82)	116/127 (91.34)	0.18
Hypercholesterolemia	211/307 (68.73)	85/125 (68.00)	0.88
Smoker (current or former)	140/279 (50.18)	35/116 (30.17)	<0.001
Previous PCI	110/307 (35.83)	32/126 (25.40)	0.036
Previous CABG	29/308 (9.42)	9/128 (7.03)	0.42
Previous stroke	18/309 (5.83)	6/125 (4.80)	0.67
LVEF < 50%	109/247 (44.13)	33/104 (31.73)	0.031
Hemoglobin, mg/dL	13.23 ± 2.05	11.89 ± 1.64	<0.001
Platelets, cells/mm ³	203108 ± 72452	238218 ± 70576	<0.001
Creatinine, mg/dL	1.40 ± 1.39	1.28 ± 1.09	0.053
eGFR, mL/min	67.87 ± 27.72	54.32 ± 22.57	<0.001
Glucose, mg/dL	123.51 ± 47.47	127.71 ± 61.42	0.91
Glycated hemoglobin, %	6.29 ± 1.41	6.17 ± 0.98	0.69
Total cholesterol, mg/dL	149.97 ± 35.40	176.17 ± 45.10	<0.001
LDL, mg/dL	87.36 ± 31.58	105.21 ± 42.86	0.03
HDL, mg/dL	42.75 ± 14.17	49.65 ± 15.05	0.02
Triglycerides, mg/dL	110.15 ± 58.97	134.73 ± 75.09	<0.01
HBR according to ARC-HBR criteria ²⁵	253/314 (80.57)	103/129 (79.84)	0.86
HAS-BLED score	2.41 ± 1.04	2.44 ± 0.99	0.68
PARIS bleeding score	5.58 ± 2.44	6.44 ± 2.40	0.001

Note: Values are mean ± SD or *n* (%). Bold values denote statistical significance at the *p* < 0.05 level.

Abbreviations: ARC, Academic Research Consortium; BMI, body mass index; CABG, coronary artery bypass grafting; eGFR, estimated glomerular filtration rate; HBR, high-bleeding risk; LVEF, left ventricular ejection fraction; NSTEMI, non-ST-elevation myocardial infarction; PCI, percutaneous coronary intervention; STEMI, ST-elevation myocardial infarction.

TABLE 2 Distribution of HBR criteria according to sex.

	Men (N = 314)	Women (N = 129)	p-Value
Age ≥ 75 years	174 (55.41)	88 (68.22)	0.013
OAC therapy	116 (37.2)	42 (33.1)	0.416
Anemia ^a	48 (15.29)	36 (27.91)	0.002
Transfusion within 4 weeks	6 (1.91)	3 (2.33)	0.72
Thrombocytopenia ^b	10 (3.18)	1 (0.78)	0.19
Bleeding requiring hospitalization within previous 12 months	11 (3.50)	7 (5.43)	0.43
Stroke within previous 12 months	3 (0.96)	0 (0.00)	0.56
History of intracerebral hemorrhage	4 (1.27)	1 (0.78)	1.00
Severe chronic liver disease ^c	7 (2.23)	1 (0.78)	0.45
CKD ^d	49 (15.61)	24 (18.60)	0.44
Cancer within the previous 3 years	41 (13.06)	12 (9.30)	0.27
Planned major, noncardiac surgery in the next 12 months	47 (14.97)	12 (9.30)	0.11
Glucocorticoids or NSAIDs use planned for > 30 days after PCI	6 (1.91)	2 (1.55)	1.00
Expected nonadherence to DAPT	20 (6.37)	7 (5.43)	0.71
HBR defining criteria, <i>n</i>	1.65 ± 1.00	1.76 ± 0.92	0.08

Note: Values are mean ± SD or *n* (%). Bold values denote statistical significance at the *p* < 0.05 level.

Abbreviations: CKD, chronic kidney disease; DAPT, dual antiplatelet therapy; eGFR, estimated glomerular filtration rate; HBR, high bleeding risk; NSAIDs, nonsteroidal anti-inflammatory drugs; OAC, oral anticoagulant; PCI, percutaneous coronary intervention.

^aDefined as hemoglobin < 11 g/dL.

^bDefined as platelets < 100'000/mL.

^cDefined as patients who have developed any of the following: variceal hemorrhage, ascites, hepatic encephalopathy, or jaundice.

^dDefined as eGFR < 40 mL/min.

TABLE 3 Procedural characteristics.

	Men (N = 314)	Women (N = 129)	p-Value
Treated vessel ^a			0.68
LAD	199/429 (46.39)	74/173 (42.77)	
LCx	112/429 (26.11)	41/173 (23.70)	
LM	18/429 (4.20)	10/173 (5.78)	
RCA	96/429 (22.38)	46/173 (26.59)	
Graft	4/429 (0.93)	2/173 (1.16)	
Total number of implanted DES per patient	1.67 ± 0.97	1.81 ± 1.30	0.64
DES diameter, mm	3.05 ± 0.49	2.96 ± 0.42	0.11
DES length, mm	41.49 ± 27.72	42.13 ± 35.33	0.72
Bifurcation lesion ^a	77/429 (17.95)	32/173 (18.50)	0.87
Thrombotic lesion ^a	19/429 (4.43)	11/173 (6.36)	0.31
Predilatation ^a	312/429 (72.73)	123/173 (71.10)	0.69
Postdilatation ^a	346/429 (80.65)	140/173 (80.92)	0.94
Use of intracoronary imaging	13/429 (3.03)	7/173 (4.05)	0.61

Note: Values are mean ± SD or *n* (%).

Abbreviations: DES, drug-eluting stent; LAD, left anterior descending; LCx, left circumflex artery; LM, left main; RCA, right coronary artery.

^aPercentages are calculated on total number of treated lesions.

confounders. Candidate variables, identified according to their known associations with ischemic and bleeding outcomes, were considered for selection in the multivariable Cox regression model. The complete lists of candidate variables used for the “ischemic” and “bleeding” models are reported in the Supplementary Material. The final models were then built using stepwise selection, with a significance level of $p < 0.10$ for inclusion and $p > 0.20$ for exclusion of candidate variables.

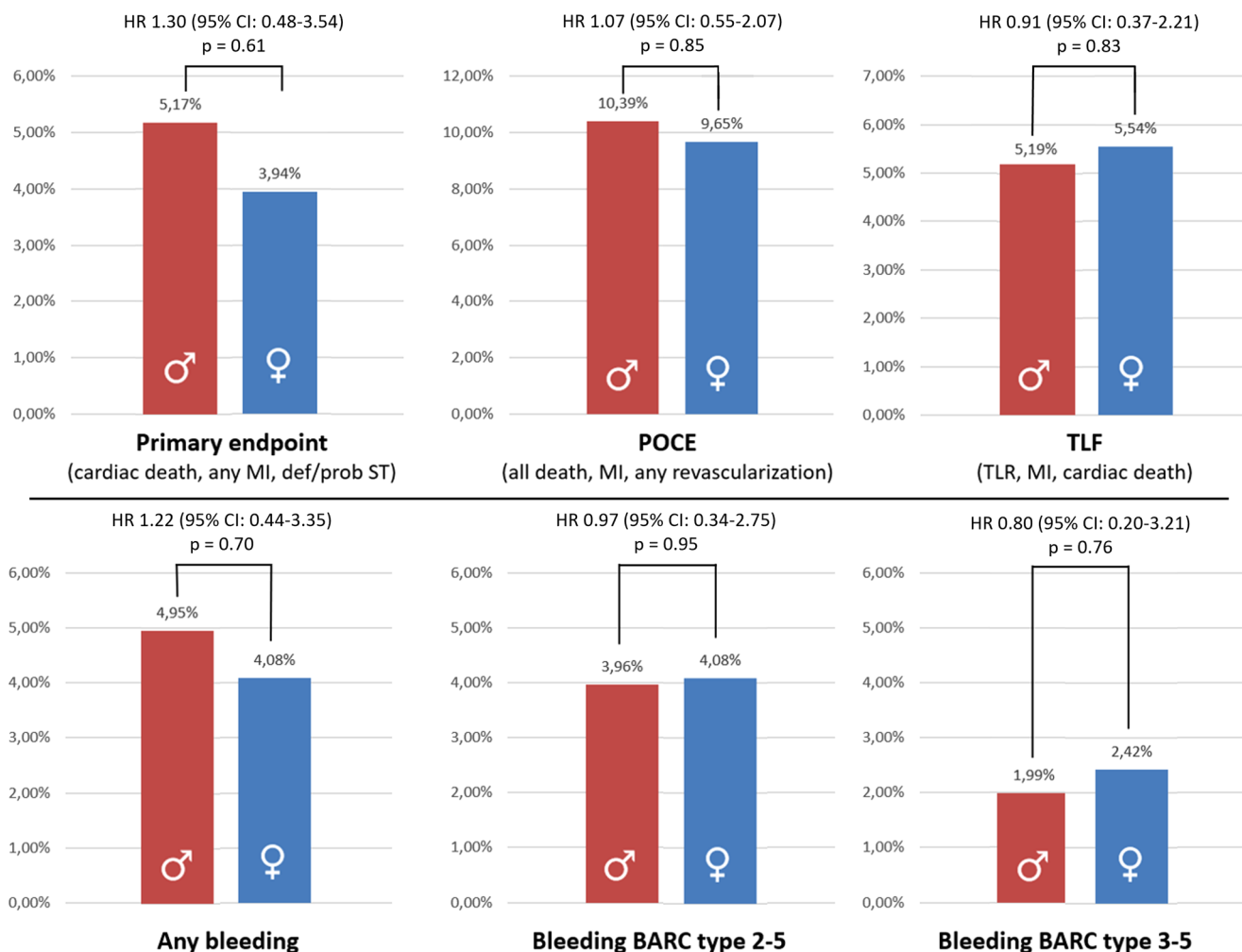
We ensured rigorous data collection and verification processes to minimize the occurrence of missing data. The accuracy and reliability of data was verified by periodic monitoring visits at each study site. We used a complete case analysis approach, where only observations with non-missing values for all variables included in the analysis were considered. This approach assumes that the data are missing completely at random and that the excluded cases do not introduce any systematic bias. Supporting Information S1: Table 1 provides detailed percentages of missing data specifically for the covariates that were utilized in the multivariate Cox analysis.

Statistical analyses were performed with STATA version 14 (Stata Corp., College Station).

3 | RESULTS

3.1 | Baseline and procedural characteristics

Table 1 reports the baseline clinical characteristics while Table 2 reports the distribution of the HBR inclusion criteria in the study participants. Of the 443 patients included in the POEM trial, 129 (29.1%) were women and 314 (70.9%) were men. Compared with men, women were older, with lower levels of hemoglobin, and worse renal function. Accordingly, they had higher PARIS bleeding score and their mean number of HBR criteria per patient tended to be higher compared with men (1.76 ± 0.92 vs 1.65 ± 1.0 ; $p = 0.08$). There were no significant differences between men and women regarding the number of patients classified as HBR according to the ARC-HBR criteria.²⁵



Abbreviations: BARC = Bleeding Academy Research Consortium, MI = myocardial infarction, POCE = patient-oriented clinical endpoint, ST = stent thrombosis, TLF = target lesion failure, TLR = target lesion revascularization.

FIGURE 1 Clinical outcomes according to sex. [Color figure can be viewed at [wileyonlinelibrary.com](https://onlinelibrary.wiley.com/doi/10.1111/j.1365-2214.2024.12527.x)]

Moreover, women had higher levels of total cholesterol, LDL, HDL, and triglycerides. Conversely, men had more frequently a history of prior PCI, reduced left ventricular ejection fraction (LVEF < 50%), lower platelet levels, and were more frequently smokers.

Procedural characteristics were comparable between men and women (Table 3). The most frequently treated vessel was the left anterior descending in both men and women, the mean diameter of the implanted stent was 2.96 ± 0.42 and 3.05 ± 0.49 mm ($p = 0.11$) and the total stent length per lesion was 42.13 ± 35.33 and 41.49 ± 27.72 ($p = 0.72$), respectively.

The specific antiplatelet therapy regimens at discharge after the index PCI are detailed in Supporting Information S1: Table 2, along with information on other medications.

3.2 | Clinical outcomes by sex

One-year follow-up was performed in 96% of patients, with a median follow-up of 366 days (IQR, 365–377). At 1-year follow-up, the risk for the primary endpoint did not significantly differ between sexes, occurring in 5.17% of men and 3.94% of women (HR 1.30; 95% CI: 0.48–3.54, $p = 0.61$; Figure 1). Equally, no significant differences were found

concerning any of the ischemic or hemorrhagic secondary endpoints (Table 4 and Figures 1 and 2). Both BARC type 2 to 5 and BARC type 3 to 5 bleedings occurred similarly in the two groups (HR 0.97; 95% CI: 0.34–2.75; $p = 0.95$ and HR 0.80; 95% CI: 0.20–3.21; $p = 0.76$, respectively). Mortality (all causes and cardiovascular) was comparable between men and women and the rate of 1-year POCE did not significantly differ between sexes (HR 1.07; 95% CI: 0.55–2.07; $p = 0.85$). Additionally, multivariate analysis did not reveal significant differences between men and women regarding all analyzed endpoints (Table 4 and Figure 3).

Early BARC type 2 to 5 bleedings within 30 days after the index PCI were rare, occurring in 5 out of 314 men and 1 out of 129 woman ($p = 0.47$). Notably, these early bleeding events did not impact the 1-year primary endpoint, as none of the six patients who experienced early bleeding subsequently had a primary endpoint event during the study period.

4 | DISCUSSION

This POEM substudy reports sex-specific results of HBR patients undergoing a 1-month DAPT regimen following PCI with BP-EES. The rates of ischemic and bleeding events were low, irrespective of

TABLE 4 Clinical outcomes at 1 year according to sex.

	Men (N = 314)	Women (N = 129)	HR (95% CI)	p-Value	Adjusted HR* (95% CI)	p-Value
Primary endpoint ^a	16 (5.17; 3.20– 8.31)	5 (3.94; 1.66–9.20)	1.30 (0.48– 3.54)	0.61	0.98 (0.35–2.77)	0.98
POCE ^b	32 (10.39; 7.46– 14.37)	12 (9.65; 5.60– 16.37)	1.07 (0.55– 2.07)	0.85	0.82 (0.42–1.64)	0.59
All-cause death	11 (3.61; 2.01– 6.42)	4 (3.24; 1.23– 8.41)	1.08 (0.34– 3.39)	0.90	0.80 (0.24–2.70)	0.72
Cardiovascular death	5 (1.65; 0.69–3.91)	3 (2.43; 0.79– 7.34)	0.66 (0.16– 2.74)	0.56	0.42 (0.09–1.95)	0.27
Any MI	12 (3.86; 2.21– 6.70)	3 (2.33; 0.76– 7.04)	1.63 (0.46– 5.78)	0.45	1.07 (0.29–3.98)	0.92
Definite/probable ST	3 (0.99; 0.32–3.05)	1 (0.78; 0.11 – 5.42)	1.19 (0.12– 11.49)	0.88	0.75 (0.07–8.45)	0.82
Any unplanned revascularization	15 (4.93; 3.00– 8.04)	6 (5.00; 2.28– 10.80)	0.98 (0.38– 2.55)	0.98	0.75 (0.28–2.03)	0.57
TVF ^c	18 (5.84; 3.72– 9.11)	7 (5.54; 2.68– 11.27)	1.03 (0.43– 2.46)	0.95	0.83 (0.34–2.05)	0.70
TVR	8 (2.67; 1.34–5.26)	2 (1.64; 0.41– 6.41)	1.58 (0.34– 7.45)	0.56	1.28 (0.26–6.30)	0.76
TLF ^d	16 (5.19; 3.21– 8.33)	7 (5.54; 2.68– 11.27)	0.91 (0.37– 2.21)	0.83	0.74 (0.29–1.86)	0.53
TLR	6 (2.01; 0.91–4.43)	2 (1.64; 0.41– 6.41)	1.18 (0.24– 5.85)	0.84	1.01 (0.19–5.36)	0.98
Any bleeding	15 (4.95; 3.01– 8.08)	5 (4.08; 1.72– 9.53)	1.22 (0.44– 3.35)	0.70	2.13 (0.70–6.46)	0.18
Bleeding BARC type 2 to 5	12 (3.96; 2.27– 6.88)	5 (4.08; 1.72– 9.53)	0.97 (0.34– 2.75)	0.95	1.83 (0.59–5.69)	0.29
Bleeding BARC type 3 to 5	6 (1.99; 0.90–4.38)	3 (2.42; 0.79– 7.33)	0.80 (0.20– 3.21)	0.76	2.25 (0.46–10.95)	0.31

Note: Percentages are Kaplan–Meier estimates that indicate patients who had an event up to 365 days after the index procedure. Comparisons are for women vs. men.

Abbreviations: BARC, Bleeding Academic Research Consortium; MI, myocardial infarction; PCI, percutaneous coronary intervention; POCE, patient-oriented composite endpoint; ST, stent thrombosis; TLF, target lesion failure; TLR, target lesion revascularization; TVF, target vessel failure; TVR, target vessel revascularization.

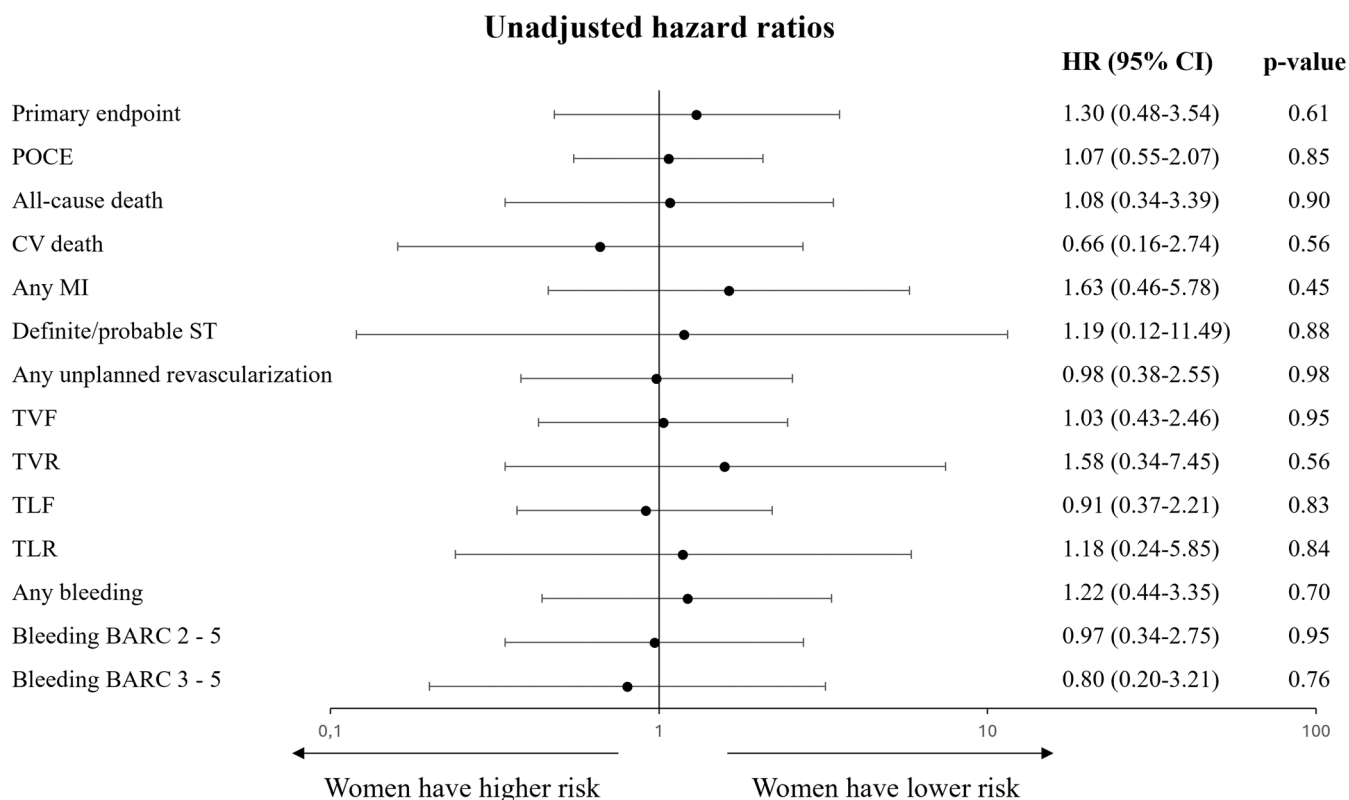
*Adjusted HRs were calculated with multivariate Cox analysis. A complete list of covariates that were used for the “ischemic” and “bleeding” Cox models, along with the list of “ischemic” and “bleeding” outcomes is reported in the Supplementary material section.

^aPrimary endpoint was a composite of cardiac death, any MI, or definite or probable stent thrombosis.

^bPatient-oriented composite endpoint was a composite of all-cause death, any MI, or any revascularization.

^cTarget vessel failure was defined as any cardiac death, target-vessel MI, or target-vessel revascularization.

^dTarget lesion failure was a composite of cardiac death, target-vessel MI, or target-lesion revascularization.



Abbreviations: BARC = Bleeding Academic Research Consortium, CV = cardiovascular, MI = myocardial infarction, POCE = patient-oriented composite endpoint, ST = stent thrombosis, TLF = target lesion failure, TLR = target lesion revascularization, TVF = target vessel failure, TVR = target vessel revascularization.

FIGURE 2 Unadjusted hazard ratios.

the sex of the participant. Our findings reassure us of the safety of this strategy also in women. This is noteworthy because ischemic heart disease represents the leading cause of death in women and accordingly the development of sex-specific strategies has been advised to improve guideline recommendations.²⁶⁻²⁸

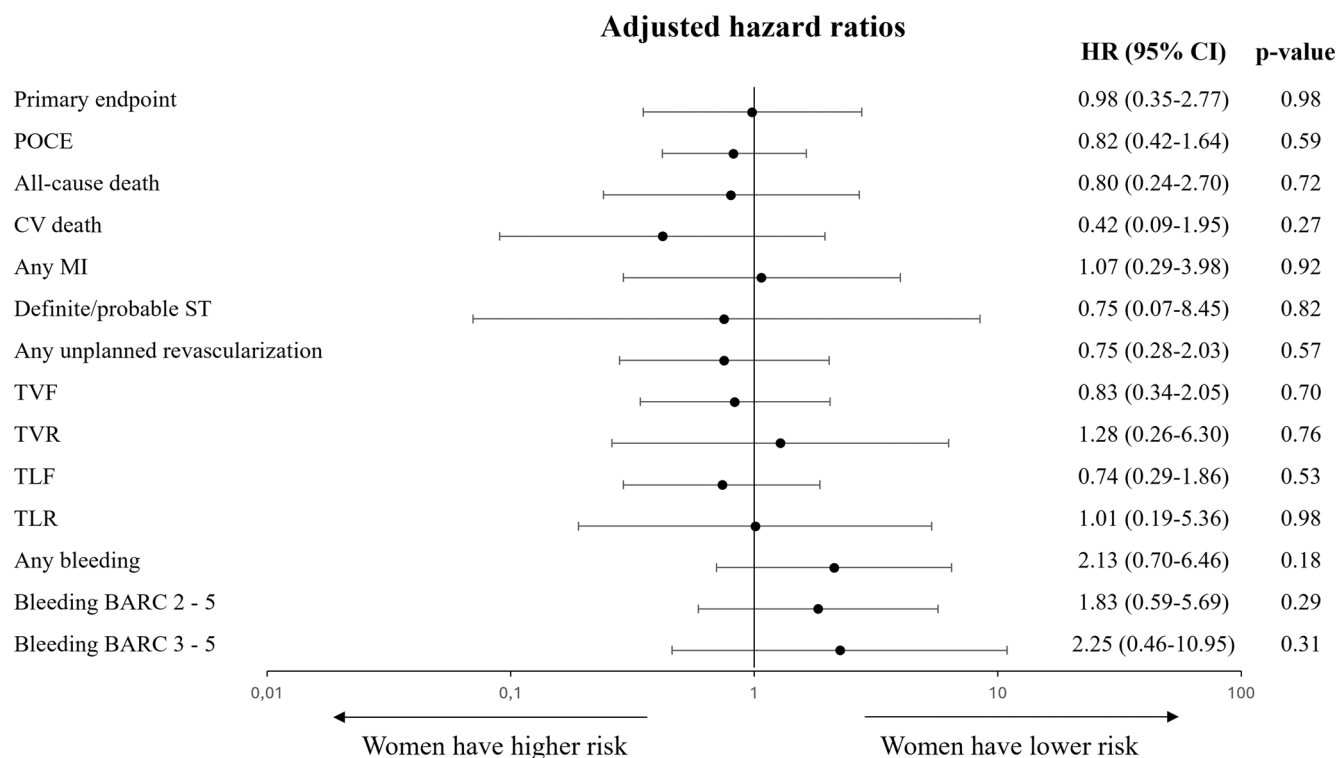
Compared to men, women undergoing PCI were often associated with poorer outcomes and a higher prevalence of risk factors associated with bleeding and ischemic events.²⁹⁻³¹ In line with our study, a European registry showed that women undergoing PCI had a higher prevalence of HBR criteria, specifically older age, anemia, chronic kidney disease (CKD), and the use of nonsteroidal anti-inflammatory drugs or corticosteroids.²⁹ Similar results were observed in an American PCI registry, in which HBR status was significantly more common among women because of anemia and CKD.³²

The sex-related subanalysis of the LEADERS-FREE trial showed that women were older, had lower levels of hemoglobin, and had worse renal function compared to men.¹⁷ The biological explanation is still unknown, but inherent physiological differences between sexes, including variations in hormonal profiles and vascular characteristics may contribute to disparities in HBR criteria prevalence. Additionally, the age-related criteria may reflect the longer life expectancy of women, potentially exposing them to age-associated health challenges. Importantly, these findings

emphasize the need for tailored risk assessment and management strategies. Recognizing and addressing the specific HBR criteria more prevalent in women can enhance the precision of clinical decisions and contribute to improved outcomes in the context of PCI, ensuring a more personalized and effective approach to women's cardiovascular health.

The debate on whether sex constitutes an independent risk factor for adverse events after PCI, and consequently, whether a short DAPT strategy has the same benefits in HBR patients of both sexes, is still ongoing. To date, sex-based differences in outcomes among HBR patients undergoing a short DAPT regimen after PCI have been reported by only a minority of studies. Of note, all of them were underpowered to assess the studied strategy among women, who represented only a minority of the total population enrolled.

The MASTER DAPT trial randomized 4579 HBR patients who underwent PCI and were uneventful after 1 month of DAPT to either short or standard DAPT. A recent sub-analysis reported similar rates of net adverse cardiovascular events (composite of ischemic and bleeding events) in men and women. However, the abbreviated DAPT regimen was more beneficial in women when evaluating the primary ischemic endpoint (a composite of all-cause death, MI, or stroke) (HR 0.68; 95% CI 0.44-1.05 for women; HR 1.17; 95% CI 0.88-1.55 for men; p for interaction = 0.04).¹⁹ On the same line of



Abbreviations: BARC = Bleeding Academic Research Consortium, CV = cardiovascular, MI = myocardial infarction, POCE = patient-oriented composite endpoint, ST = stent thrombosis, TLF = target lesion failure, TLR = target lesion revascularization, TVF = target vessel failure, TVR = target vessel revascularization.

FIGURE 3 Adjusted hazard ratios.

evidence, an individual patient data meta-analysis of randomized trials suggested that a short DAPT followed by P2Y12 monotherapy as compared with a more prolonged DAPT strategy lowers the risk of the primary ischemic endpoint (the same used in the MASTER DAPT) in women (HR 0.64; 95% CI 0.46–0.89) but not in men (HR 1.00; 95% CI 0.83–1.19; *p*-interaction = 0.02).³³ A subanalysis of the LEADERS-FREE trial, reporting sex-specific data from 2432 HBR patients randomly assigned to either biolimus-eluting stent or bare metal stent followed by a short 1-month DAPT, revealed no statistically significant differences between men and women in terms of the primary outcome (composite of cardiac death, MI, or stent thrombosis).¹⁷ We tested a 1-month DAPT strategy and applied the same inclusion criteria and identical primary outcome of the LEADERS-FREE trial. Accordingly, we observed a similar risk of ischemic events in women and men. These findings can be explained by the hypothesis that a short DAPT is particularly beneficial among women compared with men. Conversely, we did not observe the increased risk of procedural-related bleeding (namely, early and vascular access site major bleedings) evident in the LEADERS-FREE because our study participants were enrolled after the procedure. Indeed, the LEADERS-FREE included patients before the procedure to allow randomization, while in POEM patients were included after knowing the procedural results. Even if this introduces a selection bias, we believe that DAPT cannot be decided upfront, but is a dynamic

process that takes into consideration all the information, including procedural results or bleeding complications during or after PCI.

We acknowledge several limitations of our study. First, the parental trial was prematurely interrupted after the inclusion of 443 patients because of slow recruitment. Second, the absence of a comparator arm in the study design prevented a direct comparison of the short-DAPT regimen with standard care in the two sex-based subgroups. Third, inherent baseline differences between men and women could have introduced confounding biases, potentially influencing the observed outcomes. Finally, the small sample of our study provided limited statistical power, and the related risk of a type 2 error does not allow us to draw definitive conclusions. Consequently, our data should be considered hypothesis-generating, emphasizing the need for more robust and comprehensive investigations into this topic.

5 | CONCLUSION

We reported sex-wise outcomes in HBR patients treated with 1 month of DAPT following PCI with BP-EES. Our findings suggest that this strategy is particularly beneficial in women who, despite their bleeding risk profile, did not experience higher rates of adverse events compared with men. We hope our study will pave the way

toward dedicated studies on DAPT regimens in women undergoing PCI. Boston Scientific supported this study.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

AFFILIATIONS

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DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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