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Impact of Sex on 3-Year Outcome After Percutaneous Coronary Intervention Using Bare-Metal and Drug-Eluting Stents in Previously Untreated Coronary Artery Disease

Insights From the RESEARCH (Rapamycin-Eluting Stent Evaluated at Rotterdam Cardiology Hospital) and T-SEARCH (Taxus-Stent Evaluated at Rotterdam Cardiology Hospital) Registries

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Objectives We investigated the impact of sex on outcomes after percutaneous coronary intervention (PCI) with drug-eluting stent (DES).

Background Women have a higher risk of adverse outcomes after PCI than do men. However, long-term outcomes of women after contemporary PCI with DES have not been fully investigated.

Methods We performed a retrospective cohort study of 4,936 consecutive patients (28.2% women) who underwent PCIs between 2000 and 2004, before and after introduction of DES (bare-metal stent [BMS] group: n = 2,131, DES group: n = 2,805), to assess the impact of sex on long-term PCI outcomes and to compare outcome after PCI of women between the DES and BMS eras.

Results Compared with men, women undergoing PCIs were 5 years older and more frequently have comorbidities such as diabetes mellitus and hypertension. In patients treated throughout the BMS and DES eras, there were no differences by sex for risk of all-cause death, myocardial infarction, or target vessel revascularization 3 years after procedure. The procedural complexity was higher in the DES era, nevertheless, risk for target vessel revascularization and major adverse cardiac event at 3 years were significantly lower in women treated with DES than in women treated with BMS (adjusted hazard ratio [HR] for target vessel revascularization: 0.52 [95% confidence interval (CI): 0.36 to 0.75], adjusted HR for major adverse cardiac event: 0.63 [95% CI: 0.48 to 0.83]).

Conclusions Although women had worse baseline characteristics, no differences in 3-year outcomes were observed between men and women. Compared with BMS use, DES use has decreased revascularization rate equally in women and men. (J Am Coll Cardiol Intv 2009;2:603–10) © 2009 by the American College of Cardiology Foundation

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Coronary heart disease remains the leading cause of death among men and women in developed countries (1), and in Europe, around 25% of coronary revascularization is performed on women (2). In the early balloon angioplasty era, several studies found that female sex was an independent predictor of in-hospital mortality and that compared with men, women had lower rates of angiographic success, higher incidence of procedural complications and in-hospital death, and worse long-term outcomes after percutaneous

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coronary intervention (PCI) (3–5). In the bare-metal stent (BMS) era, sex-based differences in outcomes have decreased in patients undergoing PCI (6,7). In a large prospective registry study of 4,374 patients treated with BMS, women had lower rates of restenosis at 6-month angiographic follow-up compared with men, and women less frequently required target vessel revascularization (TVR) at 1 year: female sex was an independent predictor of freedom from restenosis (8). Furthermore, a recent study (9) performed in patients treated with BMS demonstrated that female sex conferred a long-term survival advantage after PCI despite the presence of higher risk characteristics.

Abbreviations and Acronyms

BMS = bare-metal stent(s)
DES = drug-eluting stent(s)
MACE = major adverse cardiac event
MI = myocardial infarction
PCI = percutaneous coronary intervention
PES = paclitaxel-eluting stent(s)
SES = sirolimus-eluting stent(s)
TIMI = Thrombolysis In Myocardial Infarction
TVR = target vessel revascularization

Clinical practice of PCI has changed since the introduction of the drug-eluting stent (DES) with a significantly lower rate of restenosis compared with BMS use (10). There is currently a paucity of published data available on the comparison of sex after PCI using DES. Pivotal trials of sirolimus-eluting stents (SES) and paclitaxel-eluting stents (PES) have included only a small number of women and were limited to patients with elective PCI and selective angiographic characteristics. In these low-risk populations, sex was not independently associated with adverse outcomes (11,12). Recently, using the National Heart, Lung, and Blood Institute (NHLBI) dynamic registry including high-risk patients, Abbott et al. (13) reported that adjusted 1-year outcomes in BMS and DES were independent of sex. However, the impact of sex on long-term outcome in unselected patients after PCI has not yet been fully investigated. Therefore, we performed an analysis using the RESEARCH (Rapamycin-Eluting Stent Evaluated at Rotterdam Cardiology Hospital) and T-SEARCH (Taxus-Stent Evaluated at Rotterdam Cardiology Hospital) registries' data to assess the impact of sex on long-term PCI outcomes and to compare outcome after PCI of women between the DES and BMS eras.

Methods

Study design and patient population. Between January 1, 2000, and December 31, 2004, 5,358 patients underwent PCI in our institution using BMS, SES, or PES. Initially, all patients were treated with BMS, but on April 16, 2002, our institution adopted the use of SES (Cypher, Cordis, Warren, New Jersey) as the default strategy for all coronary interventions, as part of the RESEARCH registry (14). On February 16, 2003, SES was replaced by PES (TAXUS, Boston Scientific, Natick, Massachusetts) as the default stent, as part of the T-SEARCH registry (15). The exclusion criteria were PCI for a lesion involving a previously implanted stent (n = 287) or patients receiving only BMS (n = 135) in the DES era, because of the unavailability of the adequate size of DES (Fig. 1). In total, 4,936 patients were included in the current study. We defined the BMS group as patients treated in a period before introduction of SES (January 2000 to April 2002, n = 2,131) and the DES group as those treated after introduction of SES (April 2002 to December 2004, n = 2,805).

Procedures and medications. All procedures were performed according to standard clinical guidelines at the time (14,15). During this period of study, primary PCI was the default strategy for all patients with ST-segment elevation myocardial infarction presenting within 6 h of symptom onset. The patients are transferred either directly by the ambulance service or by local emergency departments directly to our catheter laboratory. Angiographic success was

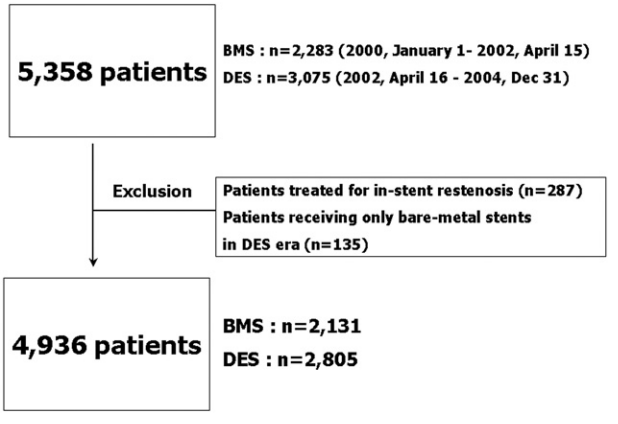

Figure 1. A Flowchart of Patient Selection

Out of 5,358 patients who underwent percutaneous intervention in a single center from 2000 to 2004, 4,936 patients were included in this analysis after exclusion of 422 patients. BMS = bare-metal stent(s); DES = drug-eluting stent(s).

defined as a residual stenosis ≤30% by visual analysis in the presence of Thrombolysis In Myocardial Infarction (TIMI) flow grade 3. All patients were pre-treated with 300 mg of clopidogrel. At least 1-month of clopidogrel treatment (75 mg/day) was recommended for patients treated with BMS. Clopidogrel was prescribed for ≥3 or 6 months for patients with SES depending of the complexity of the procedure and for ≥6 months for patients treated with PES. Life-long aspirin therapy was recommended in all patients.

End point definitions and clinical follow-up. The primary end point was major adverse cardiac event (MACE), defined as all-cause death, nonfatal myocardial infarction (MI) irrespective of the stented vessel or TVR. Secondary end points included all-cause mortality, any MI, TVR, target lesion revascularization, definite stent thrombosis, and the composites of all-cause death or nonfatal MI. Myocardial infarction was diagnosed by a rise in creatine kinase-MB >3 times the upper limit of normal (16). Target vessel revascularization was defined as a repeat revascularization of a lesion in the same epicardial vessel treated in the index procedure (17). Target lesion revascularization was defined as a repeat intervention in the stent or in the 5-mm segments proximal or distal to the stent. Hypercholesterolemia was defined as a fasting serum cholesterol level >5.5 mmol/l or use of lipid-lowering therapy at the time of the procedure. Hypertension was defined as blood pressure >140/90 mm Hg or the use of antihypertensive medications. Stent thrombosis was defined as angiographically defined thrombosis with TIMI flow grade 0 or 1 or the presence of a flow-limiting thrombus, accompanied by acute symptoms, irrespective of whether there had been an intervening reintervention (18). The timing of stent thrombosis was categorized as early (within 30 days after implantation), late (between 30 days and 1 year after implantation), or very late (more than 1 year after implantation) (19).

Follow-up data. Survival data for all patients were obtained from municipal civil registries. A questionnaire was subsequently sent to all living patients with specific questions on rehospitalization and MACE year by year. As the principal regional cardiac referral center, repeat revascularizations, either percutaneous or surgical, are normally performed at our institution and recorded prospectively in our database. For patients who suffered an adverse event at another center, medical records or discharge letters from the other institutions were systematically reviewed. General practitioners and referring physicians were contacted for additional information if necessary.

Statistical analysis. Continuous variables are presented as mean ± SD, whereas categorical variables are expressed as percentages. Statistical comparison was made between women and men and stratified by stent type (BMS and DES). Comparisons among the groups were performed by Fisher exact test for categorical variables. All statistical tests were 2-tailed, and a p value of <0.05 was considered statistically significant. The incidence of events over time was studied with the Kaplan-Meier method, and log-rank tests were applied to evaluate the difference. Patients lost to follow-up were considered at risk until the date of last contact, at which point they were censored. Cox proportional hazard methods were used to estimate unadjusted and adjusted risk ratios of clinical events at each year in relation to sex and stent type. Models were adjusted for age, cardiogenic shock, presentation with acute MI or unstable angina, hypertension, current smoking, dyslipidemia, diabetes, multivessel disease, family history of coronary artery disease, previous PCI, previous MI, previous coronary artery bypass graft, treatment of chronic total occlusion, bifurcation, bypass graft or left main lesion, American Heart Association classification B2 or C, total stented length, number of implanted stents, and recommended duration of clopidogrel. Cox proportional-hazards models adjusted with the same variables as well as stent type also were used to assess relative risks of 3-year MACE in female sex compared with male sex among patient subgroups. Statistical analysis was performed with SPSS version 12.0 for windows (SPSS Inc., Chicago, Illinois).

Results

Among 4,936 patients included in the analysis, 3,542 (71.8%) were men and 1,394 (28.2%) were women. A total of 2,131 patients received BMS (596 women and 1,535 men), and 2,805 patients were treated with DES (798 women and 2,007 men). Baseline and procedural characteristics stratified by sex and stent type are depicted in Table 1. Among patients treated with BMS, women were on average approximately 5 years older; more often had diabetes, hypertension, current smoking habit, and left main disease, and less often had previous MI. Women more often underwent PCI for unstable angina but less often for an acute MI. Recommended clopidogrel duration was longer than in men, but glycoprotein IIb/IIIa were less frequently used in women.

In demographic and procedural characteristics, differences among men and women receiving DES were similar to differences observed in patients with BMS. However, in the DES era, the rates of left main disease and duration of clopidogrel administration were comparable between men and women. Furthermore, women have lower rates of multivessel disease, bypass graft disease, and smaller diameter of stent used.

Clinical follow-up was available in 4,936 patients (98.9%: male 98.8%, female 99.3%) with a median duration of follow-up of 1,520 days. Cumulative incidences of clinical end points up to 3 years are presented in Table 2. In patients with BMS and DES, there were no differences by sex for rates of all-cause death, MI, TVR, stent thrombosis, and MACE throughout the 3 years after procedure.

Table 1. Patient Baseline Characteristics According to Sex and Stent Type

	BMS (n = 2,131)			DES (n = 2,805)				
	Women (n = 596)	Men (n = 1,535)	p Values	Women (n = 798)	Men (n = 2,007)	p Values	Women (BMS vs. DES) p Values	Men (BMS vs. DES) p Values
Age, yrs	65.5 ± 11.9	59.9 ± 11.3	<0.001	65.4 ± 11.5	60.7 ± 11.0	<0.001	0.82	0.03
Presentation SA	42.3	40.1	0.38	42.5	39.6	0.16	0.96	0.76
Presentation UA	41.6	33.9	0.001	35.5	28.7	0.001	0.02	0.001
Presentation acute MI	16.1	26.0	<0.001	22.1	31.4	<0.001	0.006	<0.001
Cardiogenic shock	1.0	1.1	1.0	2.3	2.2	1.0	0.1	0.01
Diabetes mellitus	16.9	11.4	0.001	20.8	14.8	<0.001	0.07	0.003
Hypertension	41.3	29.1	<0.001	53.4	36.5	<0.001	<0.001	<0.001
Hypercholesterolemia	42.1	43.2	0.66	51.4	54.1	0.21	0.001	<0.001
Family history	23.2	20.9	0.27	34.7	31.6	0.12	<0.001	<0.001
Current smoking	20.6	26.3	0.007	23.7	27.7	0.03	0.19	0.1
Previous PCI	10.2	9.8	0.75	8.3	7.0	0.26	0.22	0.053
Previous CABG	10.4	11.1	0.7	6.8	7.5	0.57	0.02	0.001
Previous MI	28.7	35.8	0.002	23.7	29.9	0.001	0.001	<0.001
Multivessel disease	50.7	54.3	0.13	48.4	55.4	0.001	0.42	0.95
Treated vessels*								
LAD	56.2	54.2	0.41	57.6	56.9	0.74	0.62	0.72
LCX	29.9	30.6	0.75	27.1	33.4	0.001	0.25	0.34
RCA	41.6	38.9	0.26	42.4	37.4	0.016	0.78	0.28
LM	5.2	3.1	0.021	4.0	4.7	0.48	0.3	0.001
Bypass	3.9	5.3	0.18	1.5	3.9	0.001	0.008	0.02
Bifurcation	4.7	2.6	0.02	11.9	12.4	0.75	<0.001	<0.001
Lesion type†								
A	19.6	17.7	0.29	13.4	12.8	0.66	0.002	<0.001
B1	32.9	35.2	0.34	31.2	29.0	0.27	0.52	<0.001
B2	48.2	45.5	0.29	45.0	48.9	0.07	0.25	0.5
C	32.9	36.3	0.14	42.5	45.6	0.14	<0.001	<0.001
Multivessel treatment	32.6	28.7	0.08	28.6	30.5	0.32	0.11	0.89
No. of lesions intended to treat	1.79 ± 0.91	1.74 ± 0.92	0.3	1.76 ± 0.96	1.79 ± 0.97	0.59	0.66	0.47
No. of lesions successfully treated	1.74 ± 9.92	1.70 ± 0.91	0.89	1.72 ± 0.96	1.72 ± 0.98	0.97	0.68	0.31
No. of implanted stents	1.89 ± 1.26	1.83 ± 1.19	0.42	2.22 ± 1.43	2.23 ± 1.43	0.83	<0.001	<0.001
Total stented length per patient	28.8 ± 29.6	28.9 ± 20.3	0.91	41.5 ± 29.3	43.0 ± 30.7	0.22	<0.001	<0.001
Average stent diameter	3.21 ± 0.49	3.33 ± 0.51	0.72	2.85 ± 0.53	2.95 ± 0.55	<0.001	<0.001	<0.001
Chronic total occlusion	8.7	9.2	0.8	8.4	8.6	0.88	0.85	0.15
Glycoprotein IIb/IIIa	27.2	34.7	0.001	17.2	25.1	<0.001	<0.001	<0.001
Clopidogrel prescription duration, months	2.37 ± 2.69	2.25 ± 2.06	0.04	5.50 ± 2.70	5.60 ± 3.10	0.37	<0.001	<0.001
Angiographic success of all lesions	95.5	95.6	0.91	96.1	94.2	0.04	0.59	0.14

Values are expressed as % or mean ± SD.

*Expressed as percentage of patients with each vessel type, hence total >100%. †Expressed as percentage of patients with each lesion type, hence total >100%.

BMS = bare-metal stent(s); CABG = coronary artery bypass graft; DES = drug-eluting stent(s); LAD = left anterior descending artery; LCX = left circumflex artery; LM = left main; MI = myocardial infarction; PCI = percutaneous coronary intervention; RCA = right coronary artery; SA = stable angina; UA = unstable angina.

DES versus BMS in women and men. Among the subgroups of women and men, treatment for acute MI was more frequent in patients with DES than BMS. Risk factors such as hypertension, family history, and current smoking were more frequently observed in patients with DES. The procedural complexity was higher in DES, illustrated by an increase in the treatment of type C lesions and bifurcations. In DES patients, when compared with BMS patients, total stented length and number of stents increased, but the average stent diameter decreased. Rates for TVR and MACE at any time point were significantly lower in women and men treated with DES than in patients of both sexes treated with BMS (Table 2, Fig. 2). At the 3-year follow-up, definite stent thrombosis was higher in men with DES than in men treated with BMS (2.6% vs. 1.5%, log-rank: p = 0.04), whereas it was similar in women treated with DES or BMS (2.0% vs. 1.8%, p = 0.52).

Table 2. Clinical Outcomes Stratified by Sex and Stent Type

	BMS Era (n = 2,131)			DES Era (n = 2,805)				
	Women (n = 596)	Men (n = 1,535)	p Values	Women (n = 798)	Men (n = 2,007)	p Values	Women (DES vs. BMS) p Values	Men (DES vs. BMS) p Values
At 1 year (cumulative)								
Death	8.0	6.0	0.1	6.8	5.3	0.13	0.39	0.35
Myocardial infarction	3.1	3.3	0.86	2.7	3.2	0.54	0.64	0.77
Target vessel revascularization	11.1	10.0	0.48	6.7	6.2	0.65	**0.005**	**0.0001**
Major adverse cardiac events	19.1	16.5	0.16	14.4	12.2	0.12	**0.02**	**0.0004**
Definite stent thrombosis	1.8	1.3	0.43	1.1	1.7	0.31	0.37	0.34
At 2 years (cumulative)								
Death	9.2	8.4	0.55	8.5	7.5	0.38	0.62	0.32
Myocardial infarction	3.9	4.0	0.94	3.3	3.7	0.56	0.54	0.74
Target vessel revascularization	12.8	12.8	0.96	8.2	8.4	0.88	**0.006**	**<0.0001**
Major adverse cardiac events	22.3	21.3	0.55	17.4	16.4	0.46	**0.02**	**0.0002**
Definite stent thrombosis	1.8	1.5	0.58	1.4	2.3	0.16	0.63	0.07
At 3 years (cumulative)								
Death	11.6	11.0	0.65	10.2	9.5	0.52	0.44	0.18
Myocardial infarction	4.3	4.3	0.95	4.6	4.4	0.96	0.91	0.98
Target vessel revascularization	14.7	13.9	0.63	10.3	9.7	0.72	**0.02**	**0.0001**
Major adverse cardiac events	25.9	24.5	0.45	20.9	19.1	0.27	**0.03**	**0.0001**
Definite stent thrombosis	1.8	1.5	0.66	2.0	2.6	0.62	0.52	**0.04**

Bold values are statistically significant.
Abbreviations as in Table 1.

Multivariate analyses. Unadjusted and adjusted models stratified by stent type showed that female sex did not confer a benefit or risk for any adverse events (Table 3), whereas the use of DES was associated with a lower risk of TVR or MACE in men and women at 1-, 2-, and 3-year follow-ups.

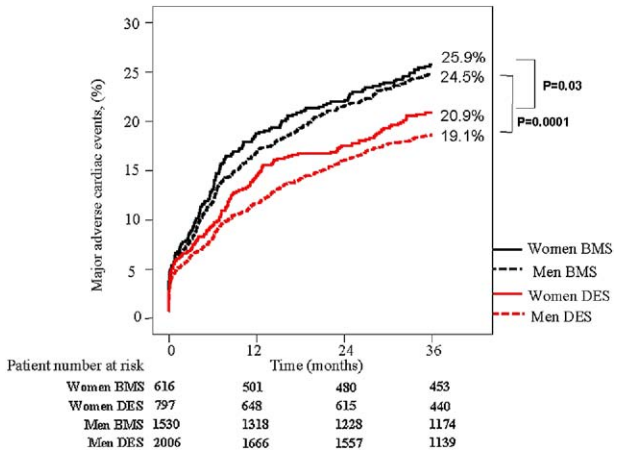

Figure 2. Kaplan-Meier Curve of MACE up to 3 Years After Index Procedure Among 4 Groups

Major adverse cardiac event (MACE) rates were significantly lower in women **(solid red line)** and men **(dotted red line)** treated with DES than in patients of both sexes treated with BMS (**solid black line** for women, **dotted black line** for men). Abbreviations as in Figure 1.

At 3 years, the risk of definite stent thrombosis was higher in men with DES versus BMS in univariate analysis (hazard ratio [HR]: 1.7 [95% confidence interval (CI): 1.03 to 2.81]); this difference was not significant in the adjusted model (adjusted HR: 1.83 [95% CI: 0.93 to 3.59]).

Figure 3 represents the results of subgroup multivariate analysis of the association between sex and the risk of MACE at 3-year follow-up in patients treated with DES. Female sex did not confer a benefit or risk for MACE in any groups except for the subpopulation presenting with acute MI (adjusted HR women vs. men: 1.37 [95% CI: 1.02 to 1.85]).

Discussion

The main findings of the current analysis from the T-SEARCH and RESEARCH registries with respect to sex are as follows: 1) DES use was associated with lower rates of TVR or MACE in both sexes; 2) after stratification for stent type, all clinical end points at any time points up to 3 years were similar between both sexes; and 3) in the subpopulation of patients presenting with acute MI, the risk of MACE at 3 years was higher in women than in men.

Only few data are available regarding sex differences in the DES era. In the TAXUS-IV–2 Year Data (TAXUS-IV) trial, they found that women had more comorbidities and an overall higher rate of repeat PCI than men did (7.6% vs. 3.2%, p = 0.03), but the restenosis rates and late loss

Table 3. Unadjusted and Adjusted HR for Sex (Women vs. Men) in Each Stent Type or for Stent Type (DES vs. BMS) in Each Sex

	HR Women vs. Men		HR DES vs. BMS		
	BMS	DES	Women	Men	p Value for Interaction Between Sex and Stent Type
At 1 year					
Death	1.34 (0.94–1.90)	1.29 (0.93–1.79)	0.84 (0.57–1.25)	0.88 (0.66–1.16)	
Adjusted	1.15 (0.75–1.75)	1.16 (0.78–1.72)	0.68 (0.40–1.15)	0.79 (0.53–1.17)	0.73
Myocardial infarction	0.95 (0.55–1.63)	0.86 (0.53–1.42)	0.86 (0.46–1.61)	0.95 (0.65–1.38)	
Adjusted	0.78 (0.41–1.47)	1.08 (0.64–1.83)	0.70 (0.32–1.53)	0.77 (0.46–1.29)	0.73
Target vessel revascularization	1.11 (0.83–1.50)	1.08 (0.78–1.50)	**0.59 (0.41–0.86)**	**0.61 (0.48–0.78)**	
Adjusted	1.13 (0.83–1.56)	1.16 (0.81–1.64)	**0.44 (0.28–0.69)**	**0.60 (0.44–0.80)**	0.89
Major adverse cardiac events	1.18 (0.94–1.47)	1.19 (0.95–1.49)	**0.74 (0.57–0.95)**	**0.73 (0.61–0.87)**	
Adjusted	1.09 (0.85–1.40)	1.23 (0.96–1.58)	**0.58 (0.42–0.80)**	**0.66 (0.52–0.84)**	0.35
Definite stent thrombosis	1.36 (0.63–2.93)	0.69 (0.33–1.43)	0.66 (0.27–1.63)	1.32 (0.75–2.32)	
Adjusted	1.25 (0.54–2.87)	0.71 (0.33–1.55)	0.50 (0.16–1.58)	1.42 (0.67–3.00)	0.1
At 2 years					
Death	1.10 (0.80–1.52)	1.14 (0.85–1.52)	0.91 (0.64–1.31)	0.89 (0.70–1.12)	
Adjusted	0.90 (0.62–1.31)	1.02 (0.73–1.43)	0.75 (0.45–1.24)	0.88 (0.64–1.21)	0.81
Myocardial infarction	0.98 (0.60-1.61)	0.87 (0.55–1.38)	0.84 (0.47–1.48)	0.94 (0.67–1.33)	
Adjusted	0.88 (0.50–1.54)	1.02 (0.63–1.66)	0.72 (0.35–1.48)	0.85 (0.52–1.38)	0.75
Target vessel revascularization	1.01 (0.77–1.32)	0.98 (0.73–1.31)	**0.63 (0.44–0.88)**	**0.64 (0.52–0.80)**	
Adjusted	1.02 (0.76–1.37)	1.07 (0.78–1.46)	**0.46 (0.31–0.69)**	**0.61 (0.47–0.79)**	0.88
Major adverse cardiac events	1.06 (0.87–1.30)	1.08 (0.88–1.32)	**0.76 (0.60–0.96)**	**0.75 (0.64–0.87)**	
Adjusted	0.98 (0.78–1.23)	1.10 (0.88–1.38)	**0.58 (0.43–0.78)**	**0.70 (0.57–0.86)**	0.42
Definite stent thrombosis	1.24 (0.58–2.62)	0.63 (0.32–1.22)	0.81 (0.34–1.91)	1.59 (0.94–2.68)	
Adjusted	1.18 (0.53–2.66)	0.72 (0.36–1.43)	0.58 (0.20–1.68)	1.70 (0.84–3.44)	0.23
At 3 years					
Death	1.07 (0.80–1.42)	1.09 (0.84–1.42)	0.88 (0.64–1.22)	0.87 (0.70–1.07)	
Adjusted	0.84 (0.61–1.17)	0.92 (0.68–1.25)	0.77 (0.49–1.20)	0.87 (0.66–1.15)	0.92
Myocardial infarction	0.99 (0.62–1.58)	1.01 (0.68–1.51)	1.03 (0.61–1.75)	1.00 (0.72–1.38)	
Adjusted	0.90 (0.53–1.53)	1.22 (0.79–1.87)	0.89 (0.47–1.70)	0.90 (0.57–1.41)	0.76
Target vessel revascularization	1.07 (0.82–1.38)	1.05 (0.80–1.38)	**0.67 (0.49–0.92)**	**0.68 (0.55–0.83)**	
Adjusted	1.08 (0.82–1.43)	1.16 (0.87–1.54)	**0.52 (0.36–0.75)**	**0.65 (0.51–0.83)**	0.87
Major adverse cardiac events	1.08 (0.89–1.30)	1.11 (0.92–1.33)	**0.78 (0.62–0.97)**	**0.75 (0.65–0.87)**	
Adjusted	0.97 (0.79–1.20)	1.11 (0.90–1.37)	**0.63 (0.48–0.83)**	**0.71 (0.59–0.86)**	0.41
Definite stent thrombosis	1.18 (0.56–2.49)	0.87 (0.50–1.51)	1.30 (0.59–2.83)	**1.7 (1.03–2.81)**	
Adjusted	1.15 (0.51–2.55)	1.01 (0.57–1.79)	0.94 (0.37–2.39)	1.83 (0.93–3.59)	0.51

Values are hazard ratio (95% confidence interval) or p value. **Bold** values are statistically significant.
HR = hazard ratio; other abbreviations as in Table 1.

were similar by sex in the DES arm of the study (11). In a pooled analysis of 1,748 patients from 4 randomized SES versus BMS trials, Solinas et al. (12) reported that despite less favorable baseline characteristics in women compared with men, at 1 year, the clinical benefits of SES were independent of sex, with reductions of binary restenosis both in women (6.3% vs. 43.8%) and in men (6.4% vs. 35.6%). Recently, using data from NHLBI dynamic registry, including high-risk patients, Abbott et al. (13) reported that patients with DES had a lower rate of repeat PCI in both sexes (14.1% in women vs. 9.5%, p = 0.02; 12.0% in men vs. 8.8%, p = 0.02) at 1 year. Our findings not only confirm the results of previous studies but also suggest that this superiority of DES to lower revascularization is maintained in both sexes up to 3 years after procedure.

In our analysis, women treated with DES had worse baseline demographics, including older age and higher prevalence of comorbidities, especially diabetes, which is associated with higher rates of restenosis. However, clinical outcomes were independent of sex with the benefit of DES over BMS being almost identical throughout the 3-year clinical follow-up. This is in contrast to previous PCI series that have reported an association between sex and clinical and angiographic restenosis rates (8,20), but it concurs with the data from a recent series on 3,223 patients, in which 1-year clinically driven revascularization was similar for both sexes (13).

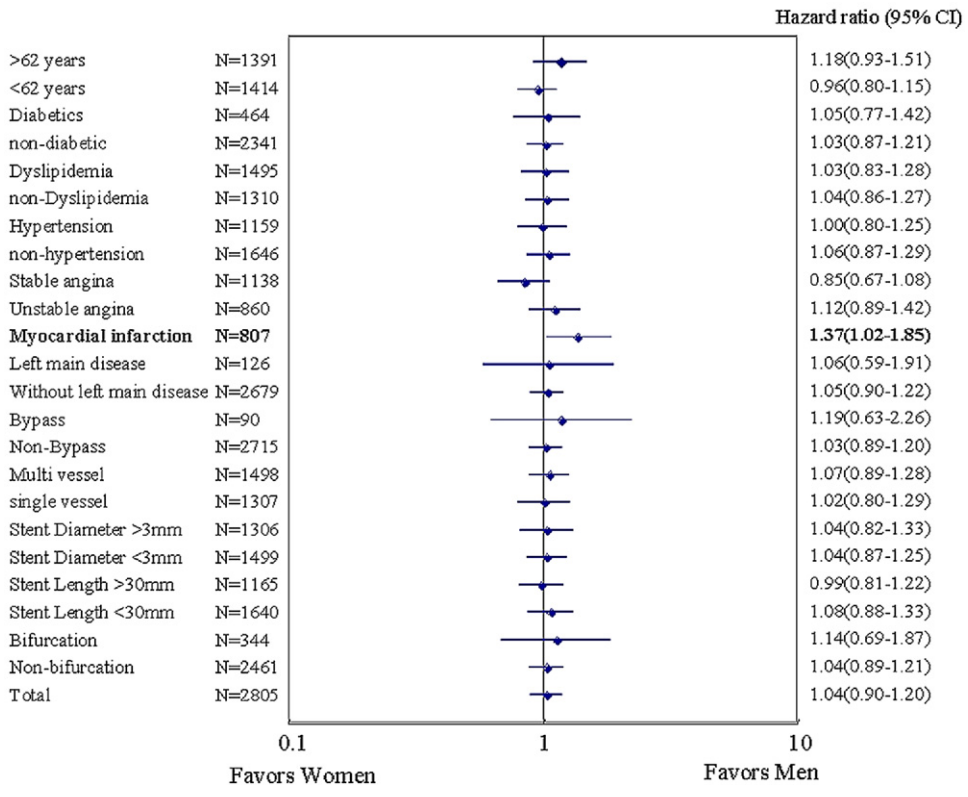

Figure 3. Adjusted Hazard Ratio of Women Versus Men on MACE at Year 3 in Subgroups

Female sex was not associated with differential MACE risk from male sex in any groups except for those presenting with acute myocardial infarction (adjusted HR women vs. men: 1.37 [95% CI: 1.02 to 1.85]). CI = confidence interval; HR = hazard ratio; other abbreviations as in Figure 2.

Our subgroup analysis suggests that women presenting with acute MI still have worse outcomes than men do. Because there were substantially fewer females than males (19.5% vs. 29.1%) in this subset, it is plausible that this inequality in proportions could be responsible for the failure to reach statistical significance for the outcomes between sexes and that even matching would have worsened the outcomes of the female cohort. In general, unadjusted comparisons of mortality after acute MI have generally indicated that women have a poorer outcome than men (21,22) and have less favorable short-term outcomes after revascularization procedures (23). In our institution, primary PCI was the default strategy for all patients with acute MI presenting within 6 h of symptom onset. Therefore, our results suggest that despite the use of DES with contemporary PCI techniques, the outcome of women with ST-segment elevation myocardial infarction still needs to be improved. In addition to anatomical differences, the basic biological differences in response to acute MI between men and women have also been suggested (24). Further investigation in this high-risk population is warranted.

Study limitations. The current study suffers from the inherent limitations of a nonrandomized trial. There were significant differences between BMS and DES and between both sexes in terms of baseline demographics. To compensate for these differences, we have performed adjustments employing multivariate analyses, although we cannot adjust confounding factors such as changes in practice during this period using various material, different guidelines, or operator's experiences. Nevertheless, these unselected patients represent real-world practice, whereas patients enrolled in clinical trials are carefully selected. In addition, we only investigated angiographically documented stent thrombosis, using a definition consistent with previous reports on stent thrombosis either after DES or BMS implantation. The latter may have led to an underestimation of the actual incidence of stent thrombosis, particularly, in patients suffering from sudden cardiac death or silent stent occlusion.

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