

Gender-Specific Outcomes After Sirolimus-Eluting Stent Implantation

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- Objectives** We examined the impact of gender on outcomes of patients undergoing percutaneous coronary intervention using sirolimus-eluting stents (SES).
- Background** Although gender-specific differences in outcome after implantation of bare-metal stents (BMS) have been described, there are no data assessing outcomes of women treated with SES.
- Methods** We performed a patient-level pooled analysis from 4 randomized SES versus BMS trials (RAVEL [Randomized Comparison of a Sirolimus-Eluting Stent with a Standard Stent for Coronary Revascularization], SIRIUS [Sirolimus-coated Bx Velocity balloon expandable stent in the treatment of patients with de novo coronary artery lesions], E-SIRIUS [Sirolimus-eluting stents for treatment of patients with long atherosclerotic lesions in small coronary arteries], and C-SIRIUS [Canadian study of the sirolimus-eluting stent in the treatment of patients with long de novo lesions in small native coronary arteries]) and analyzed outcomes as a function of gender.
- Results** Of 1,748 patients, 1,251 were men and 497 were women. A total of 878 patients were randomized to SES (629 men and 249 women), and 870 patients were randomized to BMS (622 men and 248 women). Compared with men, women were older and more frequently had diabetes mellitus, hypertension, and congestive heart failure. Although overall clinical outcomes were similar in both genders, treatment with SES was associated with significant ($p < 0.0001$) reductions in rates of in-segment binary restenosis both in women (6.3% vs. 43.8%) and in men (6.4% vs. 35.6%), resulting in a significant reduction in 1-year major adverse cardiac events, driven by a lower incidence of target lesion revascularization/target vessel revascularization in both genders. By multivariable analysis, female gender was not an independent predictor of in-segment binary restenosis or clinical outcomes regardless of stent type.
- Conclusions** In this analysis, despite less favorable baseline clinical and angiographic features in women compared with men, the angiographic and clinical benefits of SES were independent of gender. (J Am Coll Cardiol 2007;50:2111-6) © 2007 by the American College of Cardiology Foundation

Coronary artery disease is the leading cause of mortality and morbidity in women in developed countries, and a significant proportion of women require coronary revascularization (1). Several retrospective studies have focused on gender-specific differences in outcomes of patients treated with percutaneous coronary intervention (PCI). In early

angioplasty series, women compared with men had lower rates of angiographic success, higher incidence of procedural complications and in-hospital death, and worse long-term outcomes (2-4). In the same studies, female gender was identified to be an independent predictor of in-hospital mortality.

Subsequent reports of PCI in women using bare-metal stents (BMS) have provided conflicting results. Some studies have demonstrated similar rates of restenosis and clinical events in women compared with men (2-4). However, 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 those seen in men, less frequently required target vessel revascularization

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Abbreviations and Acronyms

BMS = bare metal stent(s)
CI = confidence interval
DS = diameter stenosis
HR = hazard ratio
MACE = major adverse cardiac events
MI = myocardial infarction
MLD = minimal luminal diameter
PCI = percutaneous coronary intervention
RVD = reference vessel diameter
SES = sirolimus-eluting stent(s)
TLR = target lesion revascularization
TVR = target vessel revascularization

(TVR) at 1 year, and female gender was an independent predictor of freedom from restenosis (5). In a recent report of 4,284 consecutive patients treated with PCI (77% received stents), early outcomes were quite similar between men and women, whereas at 3-year follow-up, female gender was associated with a significant reduction in the hazard of mortality (6).

Although sirolimus-eluting stents (SES) are an established treatment modality in patients undergoing PCI of native coronary vessels for stable or unstable angina and/or inducible ischemia, no specific gender-based comparisons have been reported (7-9). Therefore, we examined aggregate data from 4 randomized, controlled pivotal SES versus

BMS trials to assess the association of gender with outcomes of patients undergoing PCI using SES.

Methods

Study population. The study represents a pooled analysis of patients from the RAVEL (Randomized Comparison of a Sirolimus-Eluting Stent with a Standard Stent for Coronary Revascularization) (7), SIRIUS (SIRolImUS-coated Bx Velocity balloon expandable stent in the treatment of patients with de novo coronary artery lesions) (8), E-SIRIUS (Sirolimus-eluting stents for treatment of patients with long atherosclerotic lesions in small coronary arteries) (9), and C-SIRIUS (Canadian study of the sirolimus-eluting stent in the treatment of patients with long de novo lesions in small native coronary arteries) trials (10). Outcomes were stratified by gender and stent type (SES vs. BMS).

The study designs of individual trials have been detailed previously. In brief, in all 4 included trials, patients with stable or unstable angina or provoked ischemia and treated with PCI were randomly assigned to a sirolimus-eluting Bx Velocity stent (CYPHER, Cordis, a Johnson & Johnson Company, Warren, New Jersey) versus a control BMS of a similar design for a de novo lesion (stenosis of 51% to 99% of the luminal diameter by visual assessment on baseline angiography) in a native coronary artery. Target lesion length was <18 mm in the RAVEL trial, 15 to 30 mm in the SIRIUS trial, and 15 to 32 mm in the E-SIRIUS and C-SIRIUS trials. Stent diameters were 2.5 to 3.5 mm in the RAVEL and SIRIUS trials and 2.5 to 3.0 mm in the E-SIRIUS and C-SIRIUS trials. The use of more than 1 stent to cover the target lesion was allowed in the SIRIUS,

E-SIRIUS, and C-SIRIUS trials. In all included studies, patients were pre-treated with aspirin (81 to 325 mg) at least 12 h before PCI, and clopidogrel was administered as a loading dose of 300 mg before or immediately after PCI. Intravenous heparin was administered as boluses to maintain activated clotting time >250 s. The use of glycoprotein IIb/IIIa inhibitors was left to the discretion of operators. After the procedure, treatment with aspirin was continued indefinitely, and the recommended minimal duration of clopidogrel was 8 weeks (RAVEL, E-SIRIUS, and C-SIRIUS) or 12 weeks (SIRIUS).

End points. Definitions of major adverse cardiac events (MACE) were identical across the trials, including death, myocardial infarction (MI) (creatinine kinase greater than twice the upper limit of the normal range and an elevated level of creatine kinase-MB in the absence or presence of new pathological Q waves on the electrocardiogram for non- or Q-wave MI, respectively), and TVR (any clinically driven repeat PCI or bypass surgery of the target vessel). Target lesion revascularization (TLR) was any repeat PCI of the target lesion or bypass surgery of the target vessel performed for recurrent angina, ischemia, or diameter stenosis (DS) $\geq 70\%$ by quantitative coronary angiography. All clinical end points were adjudicated by independent clinical events committees blinded to treatment assignment.

Quantitative coronary angiography. Quantitative angiographic measurements were performed by independent angiographic core laboratories blinded to the treatment assignment (CARDIALYSIS, Rotterdam, the Netherlands, for the RAVEL trial, and Brigham and Women's Angiographic Core Laboratory, Boston, Massachusetts, for the other trials). Measurements were obtained within the stented segment (in-stent) and within the lesion segment (the stented segment as well as the margins 5 mm proximal and distal to the stent [analysis segment]). Binary restenosis at angiographic follow-up (6 months in the RAVEL trial, and 8 months in the remaining trials) was defined as a DS >50%.

Statistical analysis. Binary variables are presented as frequencies and compared using chi-square statistics or the Fisher exact test. Continuous variables are expressed as mean \pm standard deviation and compared using 2-sample *t* tests. All tests were 2-sided. Kaplan-Meier estimates were generated, and comparisons of out-of-hospital events were made using the log-rank test.

Multivariable analyses of predictors of clinical outcomes and binary angiographic restenosis were performed using Cox proportional hazards regression with stepwise selection using entry and exit criteria of $p < 0.1$ and $p < 0.2$, respectively. The variables chosen for initial entry in the models included gender, age, diabetes, hypertension, hypercholesterolemia, smoking history, indication for PCI, prior MI, prior PCI, congestive heart failure, chronic kidney disease, presence of multivessel disease, reference vessel diameter (RVD), lesion length, Thrombolysis In Myocardial Infarction flow grade 2 or 3, presence of thrombus on

baseline angiogram, left anterior descending artery target vessel, and lesion type by American Heart Association/American College of Cardiology classification.

Heterogeneity of the treatment effect on binary angiographic restenosis and individual components of MACE across the trials was tested using multivariable models with a study × treatment interaction term included, after controlling for baseline patient characteristics. For MACE, TLR, and in-stent restenosis, the p values were 0.80, 0.54, and 0.24, respectively, indicating that the treatment effect was consistent across studies with respect to these 3 outcomes.

Results

Study patients. Among the 1,748 patients included in the analysis, 1,251 (71.6%) were men and 497 (28.4%) were women. A total of 878 patients were randomized to SES (629 men [71.6%] and 249 women [28.4%]), and 870 patients were randomized to BMS (622 men [71.5%] and 248 women [28.5%]).

The demographics of the study population stratified by gender and stent type appear in Table 1. Among patients assigned to SES, women were on the average 5 years older, had a greater prevalence of comorbidities, and had a higher frequency of angina at rest, but had a lower prevalence of prior MI or prior myocardial revascularization. Among patients assigned to BMS, women differed from men in a similar fashion, except for rates of prior coronary artery bypass grafting, which were close in the 2 genders.

As shown in Table 2, among SES-treated patients, women had a higher prevalence of single-vessel disease, whereas other characteristics including RVD and lesion length were similar between the 2 genders. Among BMS-treated patients, left ventricular ejection fraction was slightly higher in women, and women had a smaller RVD and final minimal luminal diameters (MLDs), as well as longer stented segments compared with men.

Angiographic follow-up. When treated with SES, women and men had a similar late loss and binary angiographic restenosis. The patterns of in-stent restenosis and the

length of restenotic lesions did not differ significantly between women and men treated with SES, and focal in-stent restenosis was the predominant pattern of restenosis (Table 3).

When treated with BMS, women compared with men had a more prominent late loss and higher rates of angiographic restenosis. However, the patterns of restenosis were not related to gender, with the majority of restenoses demonstrating aggressive patterns (diffuse, proliferative, or total occlusion) irrespective of gender (61.4% in men and 58.5% in women, p = 0.76).

Clinical outcomes. Women and men treated with SES had similar rates of in-hospital death (0.4% vs. 0%, respectively; p = 0.28*), MI (0.8% vs. 2.7%, p = 0.11*), stent thrombosis (0% vs. 0.2%, p = 1.00*), and MACE (1.2% vs. 2.7%, p = 0.21). Similar results were observed among patients treated with BMS, with close rates of in-hospital death, stent thrombosis (no cases in either group), and TVR (0% vs. 0.2%, p = 1.00*), though there was a trend toward a higher frequency of MI among women (2.8% vs. 1.1%, p = 0.08), mainly due to procedure-related non-Q-wave MI (2.8% vs. 1.0%, p = 0.05). The Fisher exact test was used when there were <5 counts in any of the categories (indicated by p values with an asterisk [*]).

Clinical outcomes at follow-up are presented in Table 4. Among patients treated with SES, both genders had a similar incidence of 30-day and 1-year MACE. Among patients treated with BMS, women had significantly higher incidence of MI (predominantly non-Q-wave MI) at 1-year, but no significant difference in overall MACE.

SES versus BMS in women and men. Among the subgroups of women and men, baseline clinical, angiographic, and procedural characteristics were well matched between the 2 randomized treatment arms (SES and BMS). The only difference was a higher incidence of prior MI in women treated with BMS compared with SES.

At angiographic follow-up (Table 3), both genders had significantly larger MLD, smaller DS, lesser late loss, and lower rates of angiographic restenosis when treated with

Table 1 Baseline Demographic Features Stratified by Gender and Stent Type

	SES			BMS			SES vs. BMS	
	Men (n = 629)	Women (n = 249)	p Value	Men (n = 622)	Women (n = 248)	p Value	Men p Value	Women p Value
Age (mean ± SD), yrs	60.3 ± 10.9	65.7 ± 10.9	<0.0001	60.52 ± 10.41	65.42 ± 10.53	<0.0001	0.75	0.76
Hypertension, %	59.7	74.2	<0.0001	57.4	77.8	<0.0001	0.45	0.40
Hypercholesterolemia, %	72.1	67.5	0.18	70.9	74.2	0.35	0.65	0.11
Smoking, %	37.8	25.2	0.49	31.8	25.1	0.06	0.13	1.00
Diabetes mellitus, %	19.7	28.5	0.005	23.5	35.2	0.0007	0.11	0.12
Prior myocardial infarction, %	36.1	25.8	0.003	35.4	36.5	0.81	0.85	0.01
Prior PCI, %	26.6	13.7	<0.0001	23.0	16.6	0.04	0.15	0.38
Prior coronary artery bypass grafting, %	9.1	3.6	0.004	7.4	7.3	1.00	0.30	0.07
Congestive heart failure, %	2.9	7.4	0.004	4.2	9.5	0.004	0.22	0.51
Rest angina, %	18.9	29.6	0.001	18.7	29.2	0.002	0.93	1.00

BMS = bare-metal stent; PCI = percutaneous coronary revascularization; SES = sirolimus-eluting stent.

Table 2 Angiographic Features and Procedural Outcomes Stratified by Gender and Stent Type

Outcome	SES			BMS			SES vs. BMS	
	Men (n = 627)	Women (n = 247)	p Value	Men (n = 621)	Women (n = 248)	p Value	Men p Value	Women p Value
Left ventricular ejection fraction (mean ± SD), %	56.6 ± 11.1	57.9 ± 10.6	0.12	56.3 ± 10.8	59.7 ± 11.1	0.0001	0.65	0.09
Multivessel coronary disease, %	41.6	30.9	0.003	39.7	36.7	0.44	0.48	0.18
Left anterior descending artery target vessel	46.9	46.0	0.82	45.8	48.8	0.45	0.73	0.58
Lesion length (mean ± SD), mm	13.9 ± 5.6	13.8 ± 5.9	0.83	13.9 ± 5.8	13.7 ± 6.2	0.73	0.92	0.95
Baseline RVD (mean ± SD), mm	2.71 ± 0.45	2.72 ± 0.45	0.93	2.74 ± 0.49	2.66 ± 0.45	0.01	0.34	0.13
Baseline MLD (mean ± SD), mm	0.93 ± 0.36	0.97 ± 0.39	0.19	0.94 ± 0.37	0.91 ± 0.35	0.36	0.78	0.09
Baseline percent DS (mean ± SD)	65.6 ± 11.6	64.3 ± 12.8	0.18	65.7 ± 11.6	65.5 ± 11.4	0.77	0.84	0.30
Final RVD (mean ± SD), mm	2.77 ± 0.41	2.75 ± 0.42	0.59	2.79 ± 0.47	2.69 ± 0.42	0.003	0.35	0.13
Final MLD (mean ± SD), mm								
In-segment	2.27 ± 0.46	2.29 ± 0.45	0.62	2.29 ± 0.47	2.22 ± 0.45	0.056	0.46	0.11
In-stent	2.59 ± 0.41	2.57 ± 0.38	0.48	2.59 ± 0.42	2.52 ± 0.40	0.02	0.98	0.17
Final percent DS (mean ± SD)								
In-segment	18.1 ± 10.1	16.9 ± 9.2	0.09	17.9 ± 9.5	17.6 ± 9.3	0.57	0.81	0.43
In-stent	6.7 ± 8.6	7.3 ± 7.6	0.31	7.5 ± 8.6	6.4 ± 8.7	0.12	0.98	0.27
Acute gain (mean ± SD), mm								
In-segment	1.34 ± 0.48	1.32 ± 0.46	0.59	1.35 ± 0.49	1.31 ± 0.44	0.15	0.56	0.73
In-stent	1.66 ± 0.43	1.60 ± 0.43	0.08	1.65 ± 0.44	1.60 ± 0.40	0.12	0.87	0.92
Final TIMI flow grade 3, %	99.1	99.5	1.00	88.9	92.7	0.10	0.45	1.00
Stent length (mean ± SD), mm	20.9 ± 7.1	21.0 ± 7.2	0.82	20.2 ± 6.9	21.4 ± 8.0	0.04	0.10	0.54
Use of GP IIb/IIIa receptor inhibitors, %	44.0	44.6	0.93	42.4	45.7	0.40	0.60	0.85
Procedure success, %	97.6	98.4	0.61	98.7	96.8	0.08	0.20	0.25

DS = diameter stenosis; GP = glycoprotein; MLD = minimal lumen diameter; RVD = reference vessel diameter; TIMI = Thrombolysis In Myocardial Infarction; other abbreviations as in Table 1.

SES compared with BMS (for women: 86% reduction in in-lesion binary restenosis and 92% reduction in in-stent binary restenosis; for men: 82% and 93%, respectively). Rates of aggressive patterns of restenosis were remarkably lower in both genders treated with SES compared with BMS.

In women, treatment with SES versus BMS was associated with a trend toward a lower incidence of non-Q-wave MI but similar rates of MACE at 30 days and significantly lower rates of non-Q-wave MI, TLR, and/or TVR at 1 year, resulting in a highly significant (63.7%) reduction in 1-year MACE (Table 4, Fig. 1B). Treatment with SES in men was associated with a higher incidence of MI at 30 days but not at 1 year. Regardless of gender, there was a significantly lower incidence of TLR and TVR in SES-treated patients resulting in a 66.7% reduction in 1-year MACE (Table 4, Fig. 1A).

Multivariable analyses. Female gender was not associated with in-segment binary restenosis either among patients treated with SES (hazard ratio [HR] 0.63, 95% confidence interval [CI] 0.25 to 1.53, p = 0.31) or BMS (HR 1.35, 95% CI 0.91 to 1.96, p = 0.13). Among patients treated with SES, independent predictors of in-segment binary restenosis included diabetes (HR 3.00, 95% CI 1.43 to 6.31, p = 0.003) and smaller RVD (HR 5.2, 95% CI 2.12 to 12.5, p = 0.0003). Female gender was not associated with clinical

events at any time point in patients treated with either SES or BMS.

Discussion

The main findings of this pooled analysis of the outcomes of women and men treated with SES or BMS are as follows: 1) the use of SES in this clinical trial population was associated with high rates of procedural success and a low incidence of in-hospital and 30-day events in both genders; 2) when treated with SES, women and men have low and similar rates of angiographic restenosis and 1-year MACE; 3) gender, per se, was not a predictor of restenosis or MACE among patients treated with SES or BMS; and 4) treatment with BMS in women compared with men was associated with higher rates of angiographic restenosis.

In this analysis, women treated with SES had a worse baseline clinical profile, including older age and higher prevalence of comorbidities, especially diabetes mellitus that might result in higher rates of restenosis. However, angiographic and clinical outcomes were independent of gender with the magnitude of treatment benefit of SES over BMS being almost identical in both women and men. Both genders had high rates of procedural success, a low incidence of early complications, and similarly low rates of stent

Table 3 Angiographic Outcomes at Follow-Up Stratified by Gender and Stent Type

Outcome	SES			BMS			SES vs. BMS	
	Men (n = 484)	Women (n = 174)	p Value	Men (n = 494)	Women (n = 175)	p Value	Men p Value	Women p Value
RVD (mean ± SD), mm	2.73 ± 0.42	2.71 ± 0.45	0.63	2.68 ± 0.45	2.63 ± 0.43	0.22	0.06	0.08
MLD (mean ± SD), mm								
In-segment	2.07 ± 0.55	2.12 ± 0.54	0.33	1.55 ± 0.67	1.38 ± 0.68	0.006	<0.0001	<0.0001
In-stent	2.43 ± 0.54	2.40 ± 0.55	0.57	1.62 ± 0.73	1.43 ± 0.74	0.003	<0.0001	<0.0001
Percent DS (mean ± SD)								
In-segment	24.5 ± 14.7	22.1 ± 14.4	0.06	42.9 ± 21.6	47.7 ± 23.5	0.01	<0.0001	<0.0001
In-stent	11.7 ± 15.2	13.0 ± 14.5	0.30	40.1 ± 23.9	45.8 ± 25.4	0.01	<0.0001	<0.0001
Late loss, mm								
In-segment	0.17 ± 0.44	0.15 ± 0.43	0.44	0.73 ± 0.62	0.83 ± 0.67	0.07	<0.0001	<0.0001
In-stent	0.14 ± 0.42	0.15 ± 0.39	0.87	0.95 ± 0.64	1.09 ± 0.70	0.02	<0.0001	<0.0001
Binary restenosis rate, %								
In-segment	6.4	6.3	1.00	35.6	43.8	0.05	<0.0001	<0.0001
In-stent	2.3	3.4	0.40	34.2	43.2	0.03	<0.0001	<0.0001
Patterns of restenosis, %								
Focal	83.3	90.9	1.00	38.6	41.4	0.76	<0.0001	0.002
Diffuse	3.3	0.0	1.00	39.2	30.0	0.23	<0.0001	0.06
Proliferative	6.7	0.0	1.00	13.7	17.1	0.54	0.37	0.20
Total occlusion	6.7	9.1	1.00	8.5	11.4	0.47	1.00	1.00
Length of restenotic lesion (mean ± SD), mm	8.8 ± 5.4	8.9 ± 5.4	0.94	14.7 ± 7.3	15.4 ± 7.8	0.53	<0.0001	0.002

Abbreviations as in Tables 1 and 2.

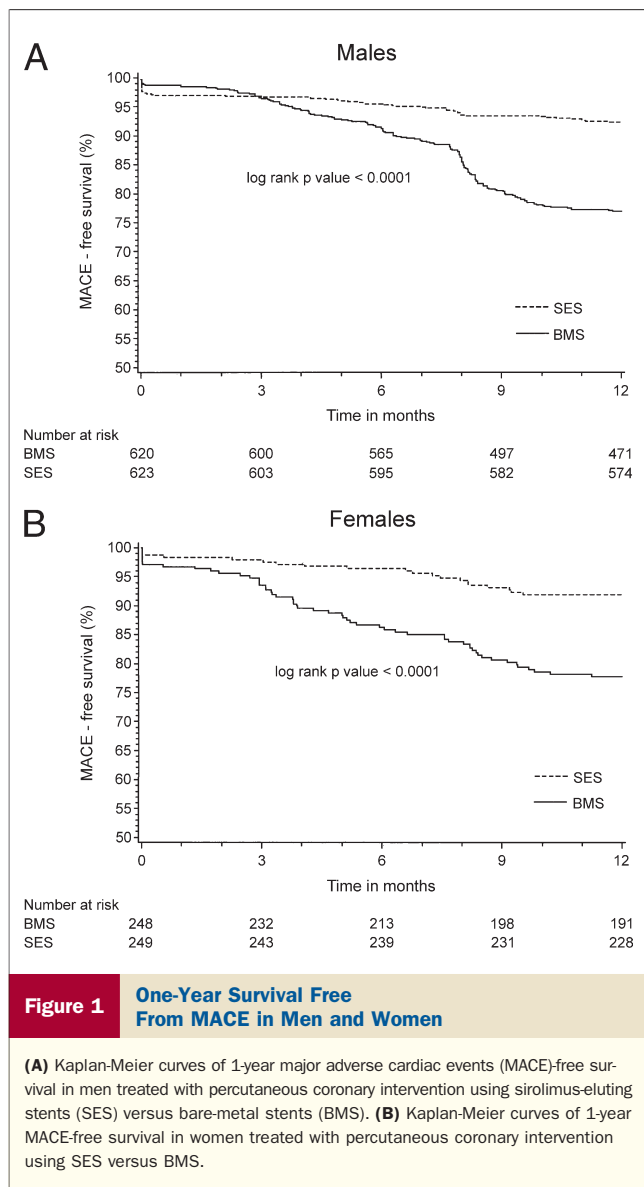
thrombosis regardless of the stent used. This is in contrast to several previous PCI series in which women compared with men had markedly lower rates of procedural success and worse in-hospital outcomes including mortality (11-13) but in accord with the data from the recent series on 1,166 consecutive patients treated with drug-eluting stents in which procedural success and in-hospital MACE were similar for both genders (14).

In this analysis, we did not find a significant difference in rates of angiographic restenosis and associated clinical events between men and women treated with SES. This is in partial agreement with a gender-based analysis from TAXUS-IV trial, which found very similar rates of angiographic restenosis in men and women treated with paclitaxel-eluting stents (15). However, in TAXUS-IV, women compared with men had approximately twice the

Table 4 Clinical Outcomes Stratified by Gender and Stent Type

Outcome	SES			BMS			SES vs. BMS	
	Men (n = 629)	Women (n = 249)	p Value	Men (n = 622)	Women (n = 248)	p Value	Men p Value	Women p Value
At 30 days (cumulative)								
Death, n (%)	0 (0.0)	1 (0.4)	0.11	1 (0.2)	0 (0.0)	0.52	0.31	0.31
Myocardial infarction, n (%)	19 (3.0)	3 (1.2)	0.12	8 (1.3)	8 (3.2)	0.06	0.03	0.12
Q-wave	5 (0.8)	1 (0.4)	0.52	1 (0.2)	0 (0.0)	0.52	0.10	0.31
Non-Q-wave	14 (2.2)	2 (0.8)	0.15	7 (1.1)	8 (3.2)	0.03	0.12	0.05
Target vessel revascularization, n (%)	5 (0.8)	1 (0.4)	0.52	2 (0.3)	0 (0.0)	0.37	0.26	0.99
Major adverse cardiac events, n (%)	19 (3.0)	4 (1.6)	0.23	9 (1.4)	8 (3.2)	0.08	0.06	0.002
Stent thrombosis, n (%)	3 (0.5)	1 (0.4)	0.88	1 (0.2)	0 (0.0)	0.52	0.32	0.31
At 1 year (cumulative)								
Death, n (%)	2 (0.3)	2 (0.8)	0.33	3 (0.5)	1 (0.4)	0.87	0.64	0.56
Myocardial infarction, n (%)	23 (3.7)	6 (2.4)	0.34	15 (2.4)	15 (6.1)	0.007	0.19	0.04
Q-wave	7 (1.1)	1 (0.4)	0.31	2 (0.3)	1 (0.4)	0.85	0.09	0.99
Non-Q-wave	16 (2.5)	5 (2.0)	0.63	13 (2.1)	14 (5.7)	0.006	0.58	0.03
Stent thrombosis, n (%)	4 (0.6)	1 (0.4)	0.67	2 (0.3)	3 (1.2)	0.11	0.41	0.31
Target lesion revascularization, n (%)	27 (4.3)	10 (4.1)	0.86	132 (21.5)	45 (18.3)	0.36	<0.0001	<0.0001
Target vessel revascularization, n (%)	35 (5.6)	17 (6.9)	0.47	147 (23.9)	50 (20.4)	0.33	<0.0001	<0.0001
Major adverse cardiac events, n (%)	48 (7.7)	20 (8.1)	0.87	143 (23.1)	55 (22.3)	0.94	<0.0001	<0.0001

Abbreviations as in Table 1.



rate of 1-year TLR (7.6% vs. 3.2%, respectively; $p = 0.03$) and TVR (10.8% vs. 5.7%, $p = 0.03$) when treated with a paclitaxel-eluting stent.

Our study also showed that both genders had a similar magnitude of treatment effect achieved with SES over BMS in reducing clinical and angiographic restenosis. When SES were used, both women and men had greater than an 80% reduction in binary angiographic restenosis and greater than a 60% reduction in 1-year TLR, TVR, and MACE. In complete agreement with data from TAXUS-IV trial, gender did not predict angiographic restenosis or MACE in either SES or BMS arm (15).

Study limitations. This post-hoc analysis was not pre-specified, and should thus be considered hypothesis-generating. Although the trials included were relatively homogeneous with respect to patient selection and treatment characteristics, variations in enrollment criteria and treatment may have influenced the results. Follow-up medications known

to improve prognosis in patients with coronary artery disease were not captured by the database, not allowing more detailed analysis of clinical outcomes in relation to gender.

Conclusions

This pooled analysis of 4 randomized trials shows that SES safely and effectively reduce clinical and angiographic restenosis in both genders. Both women and men derive similar 1-year clinical benefit from SES compared with BMS. Irrespective of stent type, female gender was not a predictor of restenosis or other associated clinical events. These data await further confirmation in unselected patients treated with SES.

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REFERENCES

1. Wenger NK, Speroff L, Packard B. Cardiovascular health and disease in women. *N Engl J Med* 1993;329:247-56.
2. Moriel M, Feld S, Almagor Y, et al. Results of coronary artery stenting in women versus men: a single center experience. *Isr Med Assoc J* 2003;5:398-402.
3. Lansky AJ. Outcomes of percutaneous and surgical revascularization in women. *Prog Cardiovasc Dis* 2004;46:305-19.
4. Argulian E, Patel AD, Abramson JL, et al. Gender differences in short-term cardiovascular outcomes after percutaneous coronary interventions. *Am J Cardiol* 2006;98:48-53.
5. Mehili J, Kastrati A, Bollwein H, et al. Gender and restenosis after coronary artery stenting. *Eur Heart J* 2003;24:1523-30.
6. Berger JS, Sanborn TA, Sherman W, et al. Influence of sex on in-hospital outcomes and long-term survival after contemporary percutaneous coronary intervention. *Am Heart J* 2006;151:1026-31.
7. Morice MC, Serruys PW, Sousa JE, et al. A randomized comparison of a sirolimus-eluting stent with a standard stent for coronary revascularization. *N Engl J Med* 2002;346:1773-80.
8. Moses JW, Leon MB, Popma JJ, et al. Sirolimus-eluting stents versus standard stents in patients with stenosis in a native coronary artery. *N Engl J Med* 2003;349:1315-23.
9. Schofer J, Schluter M, Gershlick AH, et al. Sirolimus-eluting stents for treatment of patients with long atherosclerotic lesions in small coronary arteries: double-blind, randomised controlled trial (E-SIRIUS). *Lancet* 2003;362:1093-9.
10. Schampaert E, Cohen EA, Schluter M, et al. The Canadian study of the sirolimus-eluting stent in the treatment of patients with long de novo lesions in small native coronary arteries (C-SIRIUS). *J Am Coll Cardiol* 2004;43:1110-5.
11. Robertson T, Kennard ED, Mehta S, et al. Influence of gender on in-hospital clinical and angiographic outcomes and on one-year follow-up in the New Approaches to Coronary Intervention (NACI) registry. *Am J Cardiol* 1997;80:26K-39K.
12. Alfonso F, Hernandez R, Banuelos C, et al. Initial results and long-term clinical and angiographic outcome of coronary stenting in women. *Am J Cardiol* 2000;86:1380-3.
13. Watanabe CT, Maynard C, Ritchie JL. Comparison of short-term outcomes following coronary artery stenting in men versus women. *Am J Cardiol* 2001;88:848-52.
14. Thompson CA, Kaplan AV, Friedman BJ, et al. Gender-based differences of percutaneous coronary intervention in the drug-eluting stent era. *Catheter Cardiovasc Interv* 2006;67:25-31.
15. Lansky AJ, Costa RA, Mooney M, et al. Gender-based outcomes after paclitaxel-eluting stent implantation in patients with coronary artery disease. *J Am Coll Cardiol* 2005;45:1180-5.