Catheterization and Cardiovascular Interventions 74:719–727 (2009)

Basic Science Review

Gender-Based Evaluation of the XIENCE V™ Everolimus-Eluting Coronary Stent System: Clinical and Angiographic Results from the SPIRIT III Randomized Trial

Alexandra J. Lansky,[1*] MD, FACC, Vivian G. Ng,[1] MD, Halil Mutlu,[1] MD, Ecaterina Cristea,[1] MD, Julian Benetato Guiran,[2] MD, Mark Midei,[3] MD, FACC, William Newman,[4] MD, Mark Sanz,[5] MD, Poornima Sood,[6] MD, MPhil, Julie Doostzadeh,[6] PhD, Xiaolu Su,[6] MS, Roseann White,[6] MA, Sherry Cao,[6] MS, Krishnankutty Sudhir,[6] MD, PhD, FACC, and Gregg W. Stone,[1] MD, FACC

Objectives: We evaluated the role of gender on clinical and angiographic results of the everolimus-eluting stent in the SPIRIT III trial. **Background:** The SPIRIT III trial demonstrated superior efficacy of the XIENCE V everolimus-eluting stent compared with the TAXUS paclitaxel-eluting stent. Whether these results are applicable to women is unknown. **Methods:** A total of 1,002 patients with coronary artery lesions of 28 mm or less long in 2.5–3.75 mm diameter vessels were prospectively randomized to receive percutaneous coronary intervention with either XIENCE V stent or TAXUS stent placement. Post hoc gender subset analysis was performed. **Results:** A total of 669 patients (200 women) received the XIENCE V stent, and 332 patients (114 women) were assigned to the TAXUS stent. Women were older and had more hypertension and diabetes than men. At 1 year, rates of MACE (11.1% vs. 5.7%, $P = 0.004$), TVF (13.7% vs. 7.5%, $P = 0.003$), TVR (10.8% vs. 4.6%, $P = 0.0007$), and TLR (7.2% vs. 2.7%, $P = 0.002$) were higher in women compared with men. The difference in 1 year MACE and TVF rates between men and women remained after adjusting for baseline covariates. Although the angiographic characteristics at baseline were similar among the female cohort, women assigned to XIENCE V had lower in-stent late loss (0.19 vs. 0.42 mm, $P = 0.01$) compared with women treated with the TAXUS stent. Although 30-day clinical outcomes were similar for women treated with XIENCE V and TAXUS stents, at 1 year, women with XIENCE V stents had significantly lower MACE (8.2% vs. 16.1 %, $P = 0.04$) and TVR (3.1% vs. 8.9%, $P = 0.03$) compared with those treated with TAXUS stents. Stent thrombosis rates were similar between women receiving either XIENCE V or TAXUS stents. **Conclusions:** Women in the SPIRIT III trial had inherently higher MACE and TVF rates than men. However, the angiographic and clinical benefits of using XIENCE V stents are generalizable to women.

Key words: women; drug-eluting stent; percutaneous coronary intervention

[1]Columbia University Medical Center and the Cardiovascular Research Foundation, New York, New York
[2]Brooklyn Hospital, Brooklyn, Department of Cardiology, New York
[3]St. Joseph Medical Center, Department of Cardiology, Towson, Maryland
[4]Wake Medical Center, Department of Cardiology, Raleigh, North Carolina
[5]St Patrick Hospital, Department of Cardiology, Missoula, Montana
[6]Abbott Vascular, Santa Clara, California

Grant sponsor: Abbott Vascular, Santa Clara, California.

Conflict of interest: Nothing to report.

*Correspondence to: Alexandra J. Lansky, MD, FACC, Chief Scientific Office, Cardiovascular Research Foundation, 111 E 59th Street, 12th Floor, New York, NY 10022. E-mail: alansky@crf.org

Received 11 March 2009; Revision accepted 17 March 2009

DOI 10.1002/ccd.22067
Published online 15 June 2009 in Wiley InterScience (www.interscience.wiley.com)

INTRODUCTION

Coronary artery disease is the leading cause of mortality among women [1]. Although stent implantation for elective PCI has become the treatment of choice in the US, recent studies have suggested that women receive less frequent invasive treatment than men [2–4]. It is thought that the results of conflicting studies demonstrating possible poorer long-term outcomes in women [5–7] may play a role in the referral bias; this includes increased rates of restenosis, which continues to be a major complication 6–12 months after stent placement [8]. In spite of this, treatment recommendations have been based on early studies, which have not looked at the influence of gender on outcome.

Drug-eluting stents have shown decreased rates of restenosis compared with bare-metal stents by locally delivering bioactive agents to the site of vascular injury [9–11]. The SPIRIT III trial demonstrated the superiority of the XIENCE V everolimus-eluting stent in the primary endpoint of in-segment late loss, along with improved short- and long-term outcomes compared with the paclitaxel-eluting stent, TAXUS [12]. Whether this stent is equally effective in men and women is unknown. We report the gender-based outcomes of XIENCE V stent placement when compared with the paclitaxel-eluting TAXUS stent of the SPIRIT III trial.

METHODS

The SPIRIT III study design, major inclusion and exclusion criteria, end points, definitions, and results have been previously described in detail [12]. Briefly, 1,002 patients with either 1 or 2 de novo coronary artery lesions were prospectively randomized in a single blind fashion to either an everolimus-eluting stent (XIENCE V; Abbott Vascular, Santa Clara, CA) or to a paclitaxel-eluting stent (TAXUS EXPRESS2; Boston Scientific, Natick, MA). One patient randomized to the paclitaxel-eluting stent group did not sign an informed consent, and his or her data are unavailable. Lesions were 28 mm or less in length with reference vessel diameters between 2.5 and 3.75 mm as determined by visual estimation. During randomization, patients were stratified by the presence of diabetes, planned dual-vessel treatment, and study site.

Angiographic follow-up was prespecified in 564 patients at 8 months. The primary end point was in-segment late loss at follow-up. All baseline and follow-up angiograms were analyzed at an independent core angiographic laboratory by technicians who were blinded to treatment assignments and clinical outcomes.

Clinical follow-up was scheduled for 1, 6, 8, 9 months, and then yearly for 5 years. The major secondary end point was ischemia-driven target vessel failure (TVF) adjudicated by an independent clinical events committee. Other adjudicated clinical end points included cardiac death, myocardial infarction or ischemia-driven target lesion revascularization (TLR), and major adverse cardiac events (MACE).

The SPIRIT III trial was approved by the institutional review board at each participating center, and consecutive, eligible patients signed written informed consent.

Statistical Analysis

All analyses were performed with the intent-to-treat population. Percentages are presented for categorical variables and compared using the Fischer's exact test. The mean $\pm$ one standard deviation (SD) is presented for continuous variables and compared using student *t*-test. Survival curves using all available follow-up data were also constructed for time to event analyses using Kaplan-Meier estimates and compared by the log-rank test. *P* values were two-sided. A *P* value of < 0.05 was considered statistically significant.

The impact of baseline characteristics on 8-month angiographic outcomes and 1 year clinical outcomes was evaluated with linear and logistic regression analyses, respectively. The covariates included in the regression models were age, body mass index, diabetes, hypertension requiring medications, hypercholesterolemia requiring medications, prior myocardial infarction, reference vessel diameter (RVD), and lesion length. For patients with more than one treatment lesion, one lesion was selected at random and included in the analysis. Analyses investigating the interaction between gender and treatment were also performed. All statistical analyses were performed using SAS version 9.1.3 (SAS Institute Inc, Cary, North Carolina).

RESULTS

Baseline Demographic and Angiographic Characteristics

Of the 1,001 randomized patients, 669 were assigned to the everolimus-eluting stent (including 469 [70.1%] men and 200 [29.9%] women), and 332 were assigned to the paclitaxel-eluting stent (including 218 [65.7%] men and 114 [34.3%] women). Gender differences in baseline demographics according to randomization are detailed in Table I. XIENCE V and TAXUS groups were well matched within the gender subgroups. However, overall women were older, had higher body mass indexes, more hypertension, diabetes, insulin-requiring

TABLE I. Baseline Demographics

	XIENCE V	TAXUS		XIENCE V	TAXUS		Total		
	Men	Men	*P* Value[a]	Women	Women	*P* Value	Men	Women	*P* Value
N[b]	469	218		200	114		687	314	
Age (Mean in years ± SD)	61.92 ± 10.26	61.59 ± 9.82	0.6814	66.28 ± 10.56	65.12 ± 10.66	0.3534	61.82 ± 10.11	65.86 ± 10.60	<0.0001
BMI (Mean in kg/m^2 ± SD)	30.17 ± 5.45	30.31 ± 5.35	0.7610	31.34 ± 6.80	31.14 ± 6.90	0.8077	30.21 ± 5.42	31.27 ± 6.83	0.0172
Hypertension (%)	73.3	71.4	0.6449	83.0	78.9	0.3696	72.7	81.5	0.0026
Hypercholesterolemia (%)	75.3	69.9	0.1607	71.7	74.5	0.6889	73.6	72.7	0.8158
All Diabetes mellitus (%)	26.9	23.1	0.3467	36.0	36.8	0.9033	25.7	36.3	0.0007
Insulin requiring (%)	5.3	4.2	0.5752	13.5	7.9	0.1453	5.0	11.5	0.0004
Current Smoker (%)	23.7	24.5	0.8459	22.6	18.8	0.4719	24.0	21.2	0.3711
Prior MI (%)	21.8	22.3	0.9204	15.7	9.8	0.1689	21.9	13.6	0.0022
Prior Cardiac Intervention (%)	35.0	32.1	0.4892	26.0	24.6	0.8929	34.1	25.5	0.0066
# Diseased Coronary Vessels (%)									
Single	59.9	64.2	0.3127	75.0	72.8	0.6888	61.3	74.2	<0.0001
Double	28.1	24.8	0.4065	21.0	21.9	0.8865	27.1	21.3	0.0598
Triple or More	11.9	10.6	0.7001	4.0	5.3	0.5837	11.5	4.5	0.0002
Unstable angina (%)	18.1	24.5	0.0642	20.2	26.1	0.2542	20.1	22.4	0.4450

MI, myocardial infarction.
[a]*P*-values were from post hoc analysis, unadjusted for multiple comparison, and for descriptive purpose only.
[b]*N* = Number of patients analyzed.

diabetes, and single vessel disease, but had lower rates of triple vessel disease, prior myocardial infarction, and prior cardiac interventions.

Baseline angiographic characteristics are shown in detail in Table II. XIENCE V and TAXUS treatment groups were well matched within gender subgroups. Comparing all randomized men and women, women had more left anterior descending artery and fewer left circumflex artery lesions. In addition, women had smaller vessel diameters, but similar lesion lengths compared with men. Women had lower percent diameter stenosis than men. Postprocedural angiography was similar between treatment groups; however, women had less in-segment acute gain and clinical procedural success than men.

Gender-Specific Angiographic Outcomes

Follow-up angiography results from 563 prespecified patients (including 387 [69%] men and 176 [31%] women) at 8 months are detailed in Table III. Women had smaller reference vessel and minimal lumen diameters compared with men, as expected given baseline findings. Accordingly, final percent diameter stenosis was similar between men and women. Late loss, in-segment and in-stent, was similar between men and women resulting in similar binary restenosis rates.

Gender subgroup analysis showed similar angiographic results between XIENCE V and TAXUS randomized patients. However, women receiving XIENCE V had lower in-stent late loss compared with TAXUS, and men receiving XIENCE V had lower in-segment late loss compared with TAXUS.

Gender-Specific Clinical Outcomes

At 30 days, MACE and TVF rates were similar in patients randomized to XIENCE V stent or TAXUS stent in both gender subgroups (Table IV). In general, women suffered from more MACE and TVF. The 1-year rates of MACE, TVF, target vessel revascularization (TVR), and TLR were significantly higher in women compared with men. Women performed worse than men in both XIENCE V and TAXUS arms, but the magnitude of the difference between men and women was larger in the TAXUS arm compared with the XIENCE V arm. The difference in 1-year MACE rates in women and men in the TAXUS arm was significant ($P = 0.019$), whereas the difference in 1-year MACE rates between women and men in the XIENCE V arm ($P = 0.146$) was not significant.

Among women, composite MACE and remote TVR rates were reduced in women randomized to XIENCE V compared with TAXUS at 1 year (Table IV). In

TABLE II. Baseline and Postprocedure Angiography

	XIENCE V Men	TAXUS Men	*P* Value[a]	XIENCE V Women	TAXUS Women	*P* Value	Total Men	Total Women	*P* Value
Baseline									
M[b]	550	254		222	129		804	351	
Lesion Location (%)									
LAD	38.6	39.9	0.7554	47.7	48.8	0.9118	39.0	48.1	0.0043
LCx	29.7	30.0	0.9338	22.5	24.8	0.6949	29.8	23.4	0.0268
RCA	31.5	29.6	0.6222	29.7	26.4	0.5409	30.9	28.5	0.4430
LMCA	0.2	0.4	0.5333	0.0	0.0	–	0.3	0.0	1.0000
QCA									
RVD (Mean in mm)	2.80 ± 0.46	2.83 ± 0.46	0.3115	2.69 ± 0.42	2.62 ± 0.42	0.1360	2.81 ± 0.46	2.67 ± 0.42	0.0001
MLD (Mean in mm)	0.81 ± 0.41	0.82 ± 0.40	0.7857	0.85 ± 0.41	0.85 ± 0.42	0.9729	0.81 ± 0.41	0.85 ± 0.41	0.1698
%DS	70.68 ± 13.31	70.45 ± 13.57	0.8269	68.21 ± 13.27	67.47 ± 13.57	0.6203	70.61 ± 13.39	67.93 ± 13.36	0.0019
Lsn Length (Mean in mm)	14.92 ± 5.54	14.85 ± 5.96	0.8704	14.15 ± 5.68	14.51 ± 5.16	0.5495	14.90 ± 5.67	14.28 ± 5.49	0.0827
ACC/AHA Lesion Class (%)									
A	5.9	6.4	0.8729	10.4	6.3	0.2435	6.1	8.9	0.0989
B1	37.1	35.5	0.6922	34.7	34.9	1.0000	36.6	34.8	0.5923
B2	36.9	40.2	0.3872	38.7	43.7	0.4266	38.0	40.5	0.4287
C	20.1	17.9	0.5004	16.2	15.1	0.8788	19.4	15.8	0.1580
Postprocedure									
M	306	145		121	75		451	196	
Acute gain (Mean in mm)									
In-segment	1.58 ± 0.55	1.63 ± 0.47	0.4057	1.50 ± 0.44	1.44 ± 0.51	0.4983	1.60 ± 0.53	1.48 ± 0.46	0.0180
In-stent	1.94 ± 0.51	1.96 ± 0.45	0.7417	1.86 ± 0.43	1.89 ± 0.44	0.6559	1.94 ± 0.49	1.87 ± 0.44	0.0898
N[b]	464	217		197	114		681	311	
Clinical Procedural Success (%)	99.1	98.6	0.6854	97.0	94.7	0.3673	99.00	96.10	0.0046

ACC/AHA, American College of Cardiology/American Heart Association; LAD, left anterior descending artery; LCx, left circumflex artery; RCA, right coronary artery; LMCA, left main coronary artery; MLD, mean lesion diameter; %DS, percent diameter stenosis; RVD, reference vessel diameter.

[a]*P*-values were from post hoc analysis, unadjusted for multiple comparisons, and for descriptive purpose.

[b]*M* = Number of Lesions analyzed; *N* = Number of patients analyzed.

Catheterization and Cardiovascular Interventions DOI 10.1002/ccd.
Published on behalf of The Society for Cardiovascular Angiography and Interventions (SCAI).

TABLE III. Follow-up Angiographic Data at 8 Months[a]

	XIENCE V Men	TAXUS Men	*P* Value[b]	XIENCE V Women	TAXUS Women	*P* Value	Total Men	Total Women	*P* Value
M[c]	306	145		121	75		451	196	
RVD (Mean in mm)	2.79 ± 0.45	2.83 ± 0.42	0.4402	2.73 ± 0.39	2.68 ± 0.42	0.5024	2.80 ± 0.44	2.71 ± 0.40	0.0360
In-stent									
MLD (Mean in mm)	2.58 ± 0.50	2.51 ± 0.64	0.3021	2.49 ± 0.59	2.31 ± 0.66	0.1148	2.56 ± 0.54	2.43 ± 0.62	0.0250
%DS	5.07 ± 14.45	9.32 ± 20.72	0.0544	8.19 ± 20.70	12.41 ± 22.94	0.2814	6.35 ± 16.68	9.66 ± 21.52	0.0999
Late Loss	0.14 ± 0.35	0.25 ± 0.53	0.0576	0.19 ± 0.53	0.42 ± 0.52	0.0128	0.17 ± 0.41	0.27 ± 0.54	0.0552
In-segment									
MLD (Mean in mm)	2.24 ± 0.52	2.18 ± 0.58	0.3612	2.17 ± 0.56	2.00 ± 0.61	0.1140	2.22 ± 0.54	2.11 ± 0.58	0.0398
%DS	18.11 ± 13.05	21.66 ± 16.46	0.0490	20.56 ± 17.59	25.33 ± 15.90	0.1021	19.18 ± 14.24	22.23 ± 17.11	0.0601
Late Loss	0.13 ± 0.34	0.25 ± 0.49	0.0189	0.16 ± 0.51	0.29 ± 0.41	0.0996	0.17 ± 0.40	0.21 ± 0.48	0.3622
Binary Restenosis									
In-stent (%)	1.6	4.6	0.1359	4.3	8.0	0.4505	2.5	5.6	0.1019
In-segment (%)	4.0	7.4	0.1912	6.5	12.0	0.3433	5.0	8.4	0.1503

MLD, mean lesion diameter; %DS, percent diameter stenosis; RVD, reference vessel diameter.
[a]Follow-up window ±28 days.
[b]*P*-values were from post hoc analysis, unadjusted for multiple comparison, and for descriptive purpose.
[c]M = Number of lesions analyzed.

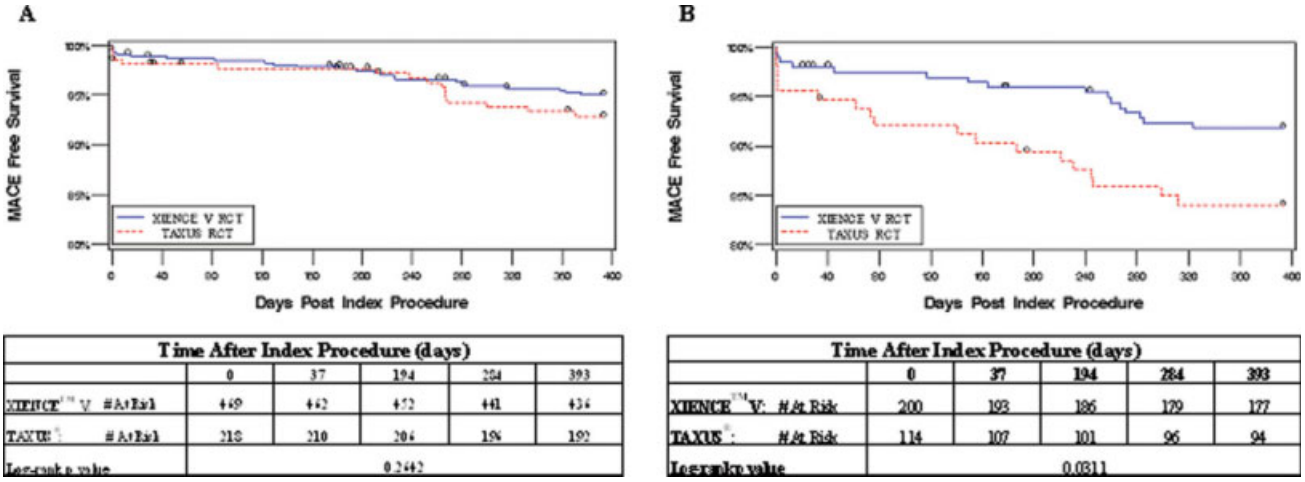
TABLE IV. Clinical Outcomes at 30 Days and 1 Year

	XIENCE V Men	TAXUS Men	*P* Value[a]	XIENCE V Women	TAXUS Women	*P* Value	Total Men	Total Women	*P* Value
N[b]	469	218		200	114		687	314	
30 days (%)[c]									
MACE	1.1	1.9	0.4740	2.0	5.3	0.1784	1.3	3.2	0.0766
TVF	1.5	1.9	0.7487	2.0	6.1	0.1057	1.6	3.5	0.0652
Cardiac death	0.0	0.0	–	0.0	0.0	–	0.0	0.0	–
Myocardial infarction	0.9	1.4	0.6845	1.5	5.3	0.0777	1.0	2.9	0.0526
TVR	0.6	0.5	1.0000	1.0	1.8	0.6241	0.6	1.3	0.2678
TLR	0.2	0.5	0.5322	1.0	0.0	0.5354	0.3	0.6	0.5938
TVR, remote	0.4	0.5	1.0000	0.0	1.8	0.1319	0.4	0.6	0.6518
Vascular Complication	0.6	0.5	1.0000	1.5	0.0	0.5563	0.6	1.0	0.6844
Stent Thrombosis	0.2	0.0	1.0000	1.0	0.0	0.5354	0.1	0.6	0.2336
1 year (%)[d]									
MACE	5.0	7.2	0.2804	8.2	16.1	0.0397	5.7	11.1	0.0036
TVF	7.4	7.7	0.8751	11.3	17.9	0.1224	7.5	13.7	0.0030
Cardiac death	0.9	1.4	0.6833	0.5	0.0	1.0000	1.0	0.3	0.4470
Myocardial infarction	2.6	2.4	1.0000	3.1	7.1	0.1529	2.5	4.6	0.1149
TVR	4.8	4.3	1.0000	9.3	13.4	0.3387	4.6	10.8	0.0007
TLR	2.2	3.8	0.3007	6.2	8.9	0.3689	2.7	7.2	0.0016
TVR, remote	3.1	1.9	0.6064	3.1	8.9	0.0340	2.7	5.2	0.0589
Vascular Complication	0.7	1.5	0.3807	1.6	1.8	1.0000	0.9	1.7	0.3348
Stent Thrombosis	0.2	0.5	0.5265	0.5	0.9	1.0000	0.3	0.7	0.5936

MACE, major adverse cardiac events; MI, myocardial infarction; TLR, target lesion revascularization; TVF, target vessel failure; TVR, target vessel revascularization.
[a]*P*-values were from post hoc analysis, unadjusted for multiple comparison, and for descriptive purpose.
[b]N = Number of patients.
[c]Follow-up window ±7 days for 30 day analysis.
[d]Follow-up window ±28 days for 1 year analysis.

addition, 1 year MACE event free survival rates were higher for women randomized to XIENCE V when compared with TAXUS (Fig. 1B, *P* log-rank = 0.03). There was also a trend toward higher 1 year TVF event free survival rates for XIENCE V women compared with TAXUS women (Fig. 2B, *P* log rank = 0.09).

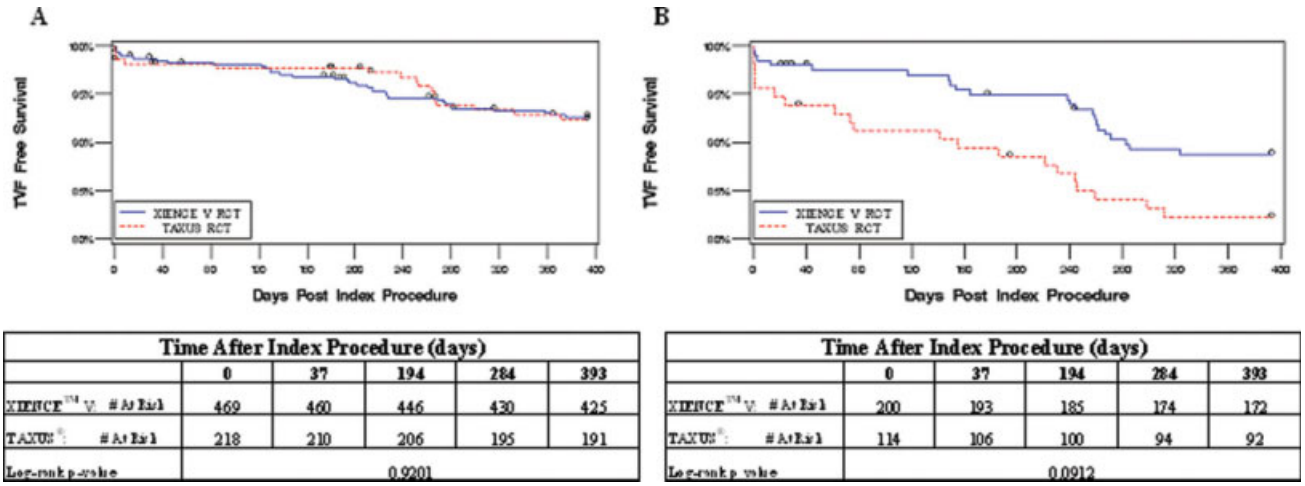
Stent thrombosis and vascular complication rates were similar in men compared with women, stent



Time After Index Procedure (days)					
	0	37	194	284	393
XIENCE V: # At Risk	469	462	452	441	436
TAXUS: # At Risk	218	210	206	196	192
Log-rank p value	0.2462				

Time After Index Procedure (days)					
	0	37	194	284	393
XIENCE V: # At Risk	200	193	186	179	177
TAXUS: # At Risk	114	107	101	96	94
Log-rank p value	0.0311				

Fig. 1. (A) Kaplan-Meier curve of 1-year major adverse cardiac events (MACE) free survival in men treated with percutaneous coronary intervention using XIENCE V versus TAXUS stents. (B) Kaplan-Meier curve of 1-year major adverse cardiac events (MACE) free survival in women treated with percutaneous coronary intervention using XIENCE V versus TAXUS stents. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]



Time After Index Procedure (days)					
	0	37	194	284	393
XIENCE V: # At Risk	469	460	446	430	425
TAXUS: # At Risk	218	210	206	195	191
Log-rank p value	0.9201				

Time After Index Procedure (days)					
	0	37	194	284	393
XIENCE V: # At Risk	200	193	185	174	172
TAXUS: # At Risk	114	106	100	94	92
Log-rank p value	0.0912				

Fig. 2. (A) Kaplan-Meier curve of 1-year target vessel failure (TVF) free survival in men treated with percutaneous coronary intervention using XIENCE V versus TAXUS stents. (B) Kaplan-Meier curve of 1-year target vessel failure (TVF) free survival in women treated with percutaneous coronary intervention using XIENCE V versus TAXUS stents. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

randomization, and within gender subgroups at both 30 days and 1 year.

Multivariable Analysis of Angiographic and Clinical Outcomes

A total of 436 patients (including 308 [70.6%] men and 128 [29.4%] women) were included in multivariable analysis of angiographic outcomes. Unadjusted models demonstrated a significant difference in in-segment late loss and percent diameter stenosis between XIENCE V and TAXUS arms that was not eliminated after adjustment for clinical comorbidities or baseline angiographic characteristics (Table V). No differences in in-segment late loss or percent diameter stenosis were found between men and women in unadjusted or covariate adjusted models. Furthermore, the test for treatment by gender interaction was not statistically significant, indicating a lack of evidence for a treatment by gender interaction effect in the linear

TABLE V. Linear Regression Analysis of Angiographic Outcomes at 8 Months

	In-segment late loss			In-segment %diameter stenosis		
Model	*P*-value for treatment[a]	*P*-value for gender	*P*-value for interaction	*P*-value for treatment	*P*-value for gender	*P*-value for interaction
Unadjusted	0.004	0.480	–	0.009	0.069	–
Model 1[b]	0.013	0.534	0.857	0.018	0.095	0.696
Model 2[c]	0.002	0.901	–	0.003	0.256	–

[a]*P*-values were from post hoc analysis and for descriptive purpose only.
[b]Model 1 includes treatment, gender, and treatment by gender interaction.
[c]Model 2 includes treatment, gender, age, body mass index, diabetes, hypertension, hypercholesterolemia, reference vessel diameter, and lesion length.

TABLE VI. Logistic Regression Analysis of Clinical Outcomes at 1 Year

	MACE			TVF		
Model	*P*-value for treatment[a]	*P*-value for gender	*P*-value for interaction	*P*-value for treatment	*P*-value for gender	*P*-value for interaction
Unadjusted	0.019	0.000	–	0.203	0.000	–
Model 1[b]	0.036	0.121	0.415	0.104	0.006	0.248
Model 2[c]	0.037	0.038	–	0.250	0.009	–

MACE, major adverse cardiac events; TVF, target vessel failure.
[a]*P*-values were from post hoc analysis and for descriptive purpose only.
[b]Model 1 includes treatment, gender, and treatment by gender interaction.
[c]Model 2 includes treatment, gender, age, body mass index, diabetes, hypertension, hypercholesterolemia, prior myocardial infarction, reference vessel diameter, and lesion length.

regression analysis of in-segment late loss and in-segment percent diameter stenosis.

All 1,001 patients (including 687 [68.6%] men and 314 [31.4%] women) were included in multivariable analysis of clinical outcomes. One year MACE rates were lower in the XIENCE V arm compared with the TAXUS arm and among men compared with women (Table VI). The differences in MACE persisted after adjusting clinical and angiographic baseline covariates. Women suffered higher rates of TVF when compared with men, which persisted with multivariable covariate adjustment; however, 1 year TVF rates were similar between XIENCE V and TAXUS patients in both the unadjusted and covariate adjusted models. Furthermore, the test for treatment by gender interaction was not statistically significant, indicating a lack of evidence for a treatment by gender interaction effect in the logistic analysis of 1 year MACE and TVF.

DISCUSSION

The results of this study of the SPIRIT III trial demonstrate that the angiographic and clinical benefits of the XIENCE V stent compared with the TAXUS stent demonstrated in SPIRIT III are applicable to women. Angiographic results at follow-up were similar between men and women with both gender subgroups showing improved late-loss outcomes. Although women overall had increased rates of MACE and TVF compared with men, women treated with the XIENCE V stent had improved angiographic and clinical outcomes compared with women treated with TAXUS stent implantation.

Previous studies have shown conflicting results regarding whether gender is an independent predictor of worse postpercutaneous coronary intervention prognoses. Some studies report that female gender in and of itself is a risk factor for worsened prognosis after coronary intervention [5–7]. However, others argue that these poorer outcomes are a result of confounding variables such as diabetes, ages, and other baseline risk factors [13–16]. Few of these reports are based on randomized trials due to the under-representation of women in these studies. Consistent with previous reports, women in this trial had increased rates of coronary risk factors including significantly higher rates of hypertension and diabetes. Baseline differences in clinical comorbidities are known to increase morbidity and mortality, and these may contribute to the differences in angiographic and clinical outcomes seen here. However, multivariable analysis in this study demonstrated that the increased age and clinical comorbidities only partially explain the worsened outcomes experienced

by women. Accounting for these baseline differences failed to completely eliminate the differential gender outcomes. Thus, this particular study suggests that female gender is a risk factor for poorer ischemic outcomes after PCI.

In addition to poorer clinical baseline characteristics, women in this study were more likely to have a smaller vessel diameter, which has also been implicated in increased rates of complications after PTCA [17]. However, this problem has largely been overcome with the development of stents with smaller diameters, and in this study, stents of varying diameters were available for use. In this study, there was no evidence that there was a difference between genders in the mean in-segment late loss and percent diameter stenosis in both unadjusted and covariate adjusted models including adjusting for differences in RVD. Nonetheless, women with XIENCE V placement had improved results with decreased in-segment lesion loss compared with those with TAXUS stents; a benefit that persisted despite adjusting the regression model for key baseline characteristics.

Several PCI studies have shown a temporal pattern of differential outcomes in women [13,17–21]. These studies report that women have increased complication rates compared with men during the first 30 days post-intervention. However, at 1 year, clinical and angiographic outcomes become equivalent or superior compared with men. Without systematic angiographic and clinical follow-up, this pattern is of unknown significance. It is possible that referral bias, in which women are less likely to be referred for angiographic follow-up for symptoms, could be partially responsible for this effect. Patients in this study were systematically followed angiographically at 8 months and also followed clinically for 1 year. Our results did not find a temporal pattern. Women had increased rates of MACE and TVF at both 30 day and 1 year follow-up time points.

Even though women had inferior clinical outcomes compared with men overall, women with XIENCE V implantation showed better clinical results than woman with TAXUS placement. XIENCE V women had decreased MACE and TVR at 1 year. Similar to two other recent studies, the benefits of drug-eluting stents can be generalized to women [22,23]. Thus, in concordance with the SPIRIT III trial, those patients with XIENCE V implantation had improved outcomes compared with TAXUS implantation.

Study Limitations

Although gender was a prespecified subgroup, the present is a post hoc subset analysis that must be considered hypothesis-generating. The number of women studied was insufficient, and the study was underpowered to definitively determine whether the XIENCE V stent reduces clinical revascularization in women. Furthermore, these results can only be applied to the patient cohort specified by the protocol of the SPIRIT III trial. For example, no conclusions can be drawn regarding the optimal treatment of women with more diffuse disease or acute myocardial infarction. In this analysis, the patients in the SPIRIT III trial have been followed through the 1 year time point, and, long-term conclusions regarding gender interactions cannot be drawn.

Clinical Implications and Conclusions

In general, women undergoing stent placement have more comorbid disease and higher long-term morbidity and mortality compared with men. Despite this, compared with women receiving TAXUS stent placement, women receiving XIENCE V placement had significantly improved in-stent late loss and survival free from MACE. Safety outcome measures were equivalent between XIENCE V and TAXUS patients. Further evaluation of the XIENCE V stent specifically in women is underway in XIENCE V SPIRIT women; an international trial is in progress, which will enroll ~2,000 women with coronary artery disease undergoing percutaneous intervention.

REFERENCES

1. Heron M. Deaths: Leading Causes for 2004. Atlanta: National Center for Health Statistics; 2007.
2. Ayanian JZ, Epstein AM. Differences in the use of procedures between men and women hospitalized for coronary disease. N Engl J Med 1991;325:221–225.
3. Maynard C, Litwin PE, Martin JS, Weaver WD. Gender differences in the treatment and outcome of acute myocardial infarction. Results from the Myocardial Infarction Triage and Intervention Registry. Arch Intern Med 1992;152:972–976.
4. Steingart RM, Packer M, Hamm P, Coglianese ME, Gersh B, Geltman EM, Sollano J, Katz S, Moye L, Basta LL. Sex differences in the management of coronary artery disease. Survival and Ventricular Enlargement Investigators. N Engl J Med 1991;325:226–230.
5. Ellis SG, Roubin GS, King SB III, Douglas JS Jr, Weintraub WS, Thomas RG, Cox WR. Angiographic and clinical predictors of acute closure after native vessel coronary angioplasty. Circulation 1988;77:372–379.
6. Watanabe CT, Maynard C, Ritchie JL. Comparison of short-term outcomes following coronary artery stenting in men versus women. Am J Cardiol 2001;88:848–852.
7. Argulian E, Patel A, Abramson JL, Kulkarni A, Champney K, Palmer S, Weintraub W, Wenger NK, Vaccarino V. Gender differences in short-term cardiovascular outcomes after percutaneous coronary interventions. Am J Cardiol 2006;98:48–53.

8. Serruys PW, Unger F, Sousa JE, et al. Comparison of coronary-artery bypass surgery and stenting for the treatment of multivessel disease. N Engl J Med 2001;344:1117–1124.
9. Marx SO, Marks AR. Bench to bedside: The development of rapamycin and its application to stent restenosis. Circulation 2001;104:852–855.
10. Suzuki T, Kopia G, Hayashi S, et al. Stent-based delivery of sirolimus reduces neointimal formation in porcine coronary model. Circulation 2001;104:1188–1193.
11. Axel DI, Kunert W, Goggelmann C, et al. Paclitaxel inhibits arterial smooth muscle cell proliferation and migration in vitro and in vivo using local drug delivery. Circulation 1997;96:636–645.
12. Stone GW, Midei M, Newman W, et al. Comparison of an everolimus-eluting stent and a paclitaxel-eluting stent in patients with coronary artery disease: A randomized trial. JAMA 2008; 299:1903–1913.
13. Arnold AM, Mick MJ, Piedmonte MR, Simpfendorfer C. Gender differences for coronary angioplasty. Am J Cardiol 1994; 74:18–21.
14. de Feyter PJ, Serruys PW, Unger F, et al. Bypass surgery versus stenting for the treatment of multivessel disease in patients with unstable angina compared with stable angina. Circulation 2002;105:2367–2372.
15. Bell MR, Grill DE, Garratt KN, Berger PB, Gersh BJ, Holmes DR Jr. Long-term outcome of women compared with men after successful coronary angioplasty. Circulation 1995;91:2876–2881.
16. Berger JS, Sanborn TA, Sherman W, Brown DL. Influence of sex on in-hospital outcomes and long-term survival after contemporary percutaneous coronary intervention. Am Heart J 2006;151:1026–1031.
17. 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.
18. Mehilli J, Kastrati A, Bollwein H, Dibra A, Schuhlen H, Dirschinger J, Schomig A. Gender and restenosis after coronary artery stenting. Eur Heart J 2003;24:1523–1530.
19. Heidland UE, Heintzen MP, Klimek WJ, Michel CJ, Strauer BE. Acute complications and restenosis in women undergoing percutaneous transluminal coronary angioplasty. Is it possible to define sex differences and to determine risk factors? J Cardiovasc Risk 1998;5:297–302.
20. Kelsey SF, James M, Holubkov AL, Holubkov R, Cowley MJ, Detre KM. Results of percutaneous transluminal coronary angioplasty in women. 1985–1986 National Heart, Lung, and Blood Institute's Coronary Angioplasty Registry. Circulation 1993;87:720–727.
21. Lansky AJ. Outcomes of percutaneous and surgical revascularization in women. Prog Cardiovasc Dis 2004;46:305–319.
22. 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;46:1180–1185.
23. Solinas E, Nikolsky E, Lansky AJ, et al. Gender-specific outcomes after sirolimus-eluting stent implantation. J Am Coll Cardiol 2007;50:2111–2116.