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The Impact of Sex Differences on Fractional Flow Reserve–Guided Percutaneous Coronary Intervention

A FAME (Fractional Flow Reserve Versus Angiography for Multivessel Evaluation) Substudy

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Objectives This study sought to evaluate the impact of sex differences on fractional flow reserve (FFR)-guided percutaneous coronary intervention (PCI).

Background The FAME (Fractional Flow Reserve Versus Angiography for Multivessel Evaluation) study demonstrated that FFR-guided PCI improves outcomes compared with an angiography-guided strategy. The role of FFR-guided PCI in women versus men has not been evaluated.

Methods We analyzed 2-year data from the FAME study in the 744 men and 261 women with multivessel coronary disease, who were randomized to angiography- or FFR-guided PCI. Statistical comparisons based on sex were stratified by treatment method.

Results Although women were older and had significantly higher rates of hypertension than men did, there were no differences in the rates of major adverse cardiac events (20.3% vs. 20.2%, $p = 0.923$) and its individual components at 2 years. FFR values were significantly higher in women than in men (0.75 ± 0.18 vs. 0.71 ± 0.17, $p = 0.001$). The proportion of functionally significant lesions ($FFR \leq 0.80$) was lower in women than in men for lesions with 50% to 70% stenosis (21.1% vs. 39.5%, $p < 0.001$) and for lesions with 70% to 90% stenosis (71.9% vs. 82.0%, $p = 0.019$). An FFR-guided strategy resulted in similar relative risk reductions for death, myocardial infarction, and repeat revascularization in men and in women. There were no interactions between sex and treatment method for any outcome variables.

Conclusions In comparison with men, angiographic lesions of similar severity are less likely to be ischemia-producing in women. An FFR-guided PCI strategy is equally beneficial in women as it is in men. (J Am Coll Cardiol Intv 2012;5:1037–42) © 2012 by the American College of Cardiology Foundation

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Historically, women have higher in-hospital mortality rates and are at increased risk for adverse outcomes than men are after percutaneous coronary intervention (PCI) for coronary artery disease (CAD) (1,2). Improvements in treatment modalities, however, have narrowed these sex-associated differences, with recent studies showing similar outcomes after PCI in women and men (3–5). Nevertheless, women are less likely to undergo invasive treatment than are men (6) and are less frequently enrolled in clinical studies evaluating coronary revascularization strategies (7).

Fractional flow reserve (FFR) is a validated method for obtaining reliable functional information of a coronary stenosis. The FAME (Fractional Flow Reserve Versus Angiography for Multivessel Evaluation) study demonstrated that FFR-guided PCI improves outcomes and saves money compared with an angiography-guided strategy in patients with multivessel CAD (8–10). However, it is unknown whether the functional significance of coronary lesions is different between women and men. Moreover, the role of FFR-guided PCI in women versus men has not been evaluated. In the current study, we performed a post hoc subanalysis of the data from the FAME study to evaluate the impact of sex differences on FFR and the benefits of FFR-guided PCI.

Abbreviations and Acronyms

CAD = coronary artery disease

DES = drug-eluting stent(s)

FFR = fractional flow reserve

MACE = major adverse cardiac event(s)

MI = myocardial infarction

PCI = percutaneous coronary intervention

Methods

Study design and population. This study was a sex-specific analysis of the 2-year results of the FAME study (10). Details regarding the design, methods, and endpoints of this prospective, multicenter, randomized clinical trial have been reported (8). In brief, 1,005 patients with multivessel CAD were randomly assigned to either angiography- or FFR-guided PCI. All patients had coronary lesions of ≥50% diameter stenosis in ≥2 major epicardial vessels, which, based on the angiographic appearance and clinical data, were felt to require PCI. Patients randomized to angiography-guided PCI underwent stenting of all indicated lesions with drug-eluting stents (DES). In patients assigned to FFR-guided PCI, FFR was measured in each diseased coronary artery and stents were placed only if the FFR was ≤0.80. Patients were excluded if they had left main CAD, prior coronary artery bypass graft surgery, a recent ST-segment elevation myocardial infarction (<5 days), cardiogenic shock, or extremely tortuous or calcified coronary arteries. The study protocol was approved by each Institutional Review Board or Ethics Committee, and each patient provided written informed consent.

Procedure and adjunctive therapy. PCI was performed according to standard coronary interventional techniques with DES, with the final interventional strategy left to the discretion of the treating physician. FFR was measured with a coronary pressure guidewire (St. Jude Medical Systems, Uppsala, Sweden) at maximum hyperemia induced by intravenous adenosine, and hyperemic pressure pullback recordings were performed as necessary (8,11). FFR was defined as the ratio between the mean distal coronary pressure and the mean aortic pressure. All patients received dual antiplatelet therapy with aspirin and clopidogrel for at least 1 year after PCI.

Endpoint. All adverse clinical events were centrally adjudicated by an independent Clinical Events Committee blinded to treatment. The primary interest of this reanalysis was the occurrence of major adverse cardiac events (MACE), a composite of all-cause death, myocardial infarction (MI), or need for repeat coronary revascularization, at 2 years after PCI in each sex. Secondary endpoints included the individual components of MACE. Details on these definitions have been described (8,10). Another main goal of this analysis was to compare FFR values between women and men with similar degrees of CAD by visual estimation.

Statistical analysis. Statistical comparisons based on sex were stratified by treatment method. Continuous variables are presented as mean ± SD, and categorical variables as numbers or percentages. Between-group differences in categorical variables were assessed using the chi-square test or Fisher exact test, as appropriate, and differences in continuous variables were assessed using Student *t* test. Analyses investigating the interaction between sex and treatment method were also performed using Breslow-Day test. Angiographic lesion severity per category and the respective FFR value of each specific lesion were plotted using a box-and-whisker plot. Survival curves were constructed using the Kaplan-Meier method and compared with the log-rank test. Patients were censored at 2 years (730 days) or when events occurred. Two-tailed p values <0.05 were considered statistically significant. All statistical analysis was performed using commercially available software (SPSS version 17 for Windows, SPSS Inc., Chicago, Illinois).

Results

Baseline characteristics and procedural results. Of the 1,005 patients included in the analysis, 744 (74%) were men and 261 (26%) were women. Baseline clinical, angiographic, and procedural characteristics according to sex and treatment method are presented in Tables 1 and 2. Compared with men, women were significantly older (68.3 ± 9.5 years vs. 63.1 ± 10.2 years, p < 0.001), had higher rates of hypertension (72.0% vs. 60.6%, p = 0.001), and had higher rates of unstable angina presentation (39.1% vs. 30.4%, p = 0.010). Vessel diameters were significantly smaller in women than in men (2.41 ± 0.62 mm vs. 2.51 ± 0.63 mm, p = 0.002). Although women had significantly fewer lesions identified for stenting (2.6 ± 0.9 vs. 2.8 ± 0.9, p = 0.012)

Table 1. Baseline Characteristics

	Total			FFR-Guided PCI (n = 509)			Angiography-Guided PCI (n = 496)		
	Men (n = 744)	Women (n = 261)	p Value	Men (n = 384)	Women (n = 125)	p Value	Men (n = 360)	Women (n = 136)	p Value
Age, yrs	63.1 ± 10.2	68.3 ± 9.5	<0.001	63.2 ± 10.4	69.3 ± 8.7	<0.001	63.0 ± 10.0	67.4 ± 10.1	<0.001
BMI, kg/m^2	28.0 ± 4.6	28.2 ± 5.4	0.728	28.0 ± 4.6	28.2 ± 5.2	0.674	28.1 ± 4.6	28.2 ± 5.7	0.941
BSA, m^2	2.01 ± 0.19	1.78 ± 0.17	<0.001	2.01 ± 0.19	1.78 ± 0.17	<0.001	2.01 ± 0.19	1.78 ± 0.17	<0.001
Angina classification*			<0.001			0.016			0.015
I	196 (26.3)	51 (19.5)		107 (27.9)	25 (20.2)		89 (24.7)	26 (19.1)	
II	263 (35.3)	72 (27.6)		136 (35.4)	34 (27.2)		127 (35.3)	38 (27.9)	
III	176 (23.7)	74 (28.7)		91 (23.7)	41 (32.8)		85 (23.6)	33 (24.3)	
IV	109 (14.7)	64 (24.5)		50 (13.0)	25 (20.0)		59 (16.4)	39 (28.7)	
Cardiovascular risk factors									
Hypertension	451 (60.6)	188 (72.0)	0.001	220 (57.3)	92 (73.6)	0.001	231 (64.2)	96 (70.6)	0.178
Dyslipidemia	528 (71.0)	200 (76.6)	0.078	274 (71.4)	92 (73.6)	0.628	254 (70.6)	108 (79.4)	0.048
Current smoker	228 (30.6)	66 (25.3)	0.102	109 (28.4)	29 (23.2)	0.257	119 (33.1)	37 (27.2)	0.211
Diabetes mellitus	179 (24.1)	69 (26.4)	0.443	92 (24.0)	31 (24.8)	0.849	87 (24.2)	38 (27.9)	0.388
Family history	288 (38.7)	107 (41.0)	0.515	150 (39.1)	55 (44.0)	0.328	138 (38.3)	52 (38.2)	0.984
Previous MI	277 (37.2)	90 (34.5)	0.428	146 (38.0)	41 (32.8)	0.293	131 (36.4)	49 (36.0)	0.941
Previous PCI	211 (28.4)	64 (24.5)	0.231	111 (28.9)	35 (28.0)	0.846	100 (27.8)	29 (21.3)	0.144
Unstable angina									
With dynamic ECG changes	109 (14.7)	55 (21.1)	0.016	53 (13.8)	20 (16.0)	0.543	56 (15.6)	35 (25.7)	0.009
Without dynamic ECG changes	117 (15.7)	47 (18.0)	0.391	57 (14.8)	20 (16.0)	0.754	60 (16.7)	27 (19.9)	0.405
Left ventricular ejection fraction, %	56.7 ± 11.6	58.5 ± 11.3	0.029	56.9 ± 11.1	58.0 ± 10.8	0.368	56.4 ± 12.1	59.0 ± 11.8	0.033
Medications									
Beta-blocker	570 (76.6)	202 (77.4)	0.797	298 (77.6)	97 (77.6)	0.999	272 (75.6)	105 (77.2)	0.701
Calcium antagonist	155 (20.8)	62 (23.8)	0.324	84 (21.9)	37 (39.6)	0.780	71 (19.7)	25 (18.4)	0.736
Nitrate	233 (31.3)	113 (43.3)	<0.001	120 (31.3)	47 (37.6)	0.189	113 (31.4)	66 (48.5)	<0.001
Antianginal medications,† n	1.29 ± 0.79	1.44 ± 0.79	0.006	1.31 ± 0.80	1.45 ± 0.77	0.085	1.27 ± 0.78	1.44 ± 0.81	0.028
ACE inhibitor or ARB	377 (50.7)	145 (55.6)	0.174	191 (49.7)	76 (60.8)	0.031	186 (51.7)	69 (50.7)	0.853
Statin	604 (81.2)	210 (80.5)	0.798	315 (82.0)	102 (81.6)	0.913	289 (80.3)	108 (79.4)	0.830
Aspirin	684 (91.9)	235 (90.0)	0.346	352 (91.7)	113 (90.4)	0.662	332 (92.2)	122 (89.7)	0.369
EQ-5D score	66.8 ± 18.4	62.4 ± 19.4	0.002	67.3 ± 18.1	64.3 ± 19.0	0.125	66.3 ± 18.9	60.1 ± 19.6	0.006
EuroSCORE	2.6 ± 2.1	4.3 ± 1.9	<0.001	2.6 ± 2.0	4.6 ± 1.9	<0.001	2.6 ± 2.2	4.0 ± 1.8	<0.001

Values are mean ± SD or n (%). *Angina was assessed according to the Canadian Cardiovascular Society Functional Classification of Angina Pectoris. †Antianginal medications included beta-blockers, calcium-antagonists, and nitrates.

ACE = angiotensin-converting enzyme; ARB = angiotensin II receptor blocker; BMI = body mass index; BSA = body surface area; ECG = electrocardiogram; EQ-5D = European Quality of Life-5 Dimensions; EuroSCORE = European System for Cardiac Operative Risk Evaluation; FFR = fractional flow reserve; MI = myocardial infarction; PCI = percutaneous coronary intervention.

and significantly lower SYNTAX (Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery) scores (13.4 ± 6.8 vs. 14.9 ± 9.2, p = 0.009) than men did, the total number (2.3 ± 1.4 vs. 2.4 ± 1.2, p = 0.207) and length (42.6 ± 27.0 mm vs. 45.6 ± 27.2 mm, p = 0.121) of stents implanted per patient were comparable between women and men.

The clinical and angiographic characteristics were well matched between those randomized to FFR-guided PCI and to angiography-guided PCI, in the population as a whole and based on sex. The procedure times required for FFR- and angiography-guided treatment were similar in both men and women. However, the volume of contrast agent (for men: 283 ± 137 ml vs. 306 ± 131 ml, p = 0.019; for women: 241 ± 115 ml vs. 293 ± 117 ml, p < 0.001), the number of DES (for men: 2.0 ± 1.2 vs. 2.8 ± 1.1, p < 0.001; for women: 1.6 ± 1.4 vs. 2.9 ± 1.2, p < 0.001), and the total stent length (for men: 40.0 ± 27.7 mm vs. 51.6 ± 25.4 mm, p < 0.001; for women: 31.7 ± 27.4 mm vs. 52.6 ± 22.3 mm, p < 0.001) were significantly lower for each sex in patients who underwent FFR-guided therapy compared with those who underwent angiography-guided therapy.

Sex differences in clinical outcomes at 2 years. Sex-specific clinical outcomes at 2-year follow-up are presented in Table 3. Men and women had similar rates of MACE (20.2% vs. 20.3%, p = 0.923), death (3.4% vs. 2.7%, p = 0.591), MI (8.1% vs. 7.7%, p = 0.837), and repeat revascularization (11.4% vs. 12.3%, p = 0.717). The event rates were not different between men and women irrespective of the treatment method. Two-year MACE-free survival rates were also

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Table 2. Angiographic Findings and Procedural Results

Characteristics	Total: Men (n = 744)	Total: Women (n = 261)	Total: p Value	FFR-Guided PCI (n = 509): Men (n = 384)	FFR-Guided PCI (n = 509): Women (n = 125)	FFR-Guided PCI (n = 509): p Value	Angiography-Guided PCI (n = 496): Men (n = 360)	Angiography-Guided PCI (n = 496): Women (n = 136)	Angiography-Guided PCI (n = 496): p Value
Diseased vessels, n			0.162			0.306			0.346
2	540 (72.6)	201 (77.0)		540 (72.6)	96 (76.8)		540 (72.6)	105 (77.2)	
3	204 (27.4)	60 (23.0)		204 (27.4)	29 (23.2)		204 (27.4)	31 (22.8)	
Lesions intended to treat, n	2.8 ± 0.9	2.6 ± 0.9	0.012	2.8 ± 1.0	2.6 ± 0.9	0.021	2.8 ± 0.9	2.7 ± 0.9	0.243
Extent of occlusion by visual estimation			0.219			0.685			0.135
50% to 70% stenosis	875/2,078 (42.1)	299/686 (43.6)		473/1,088 (43.5)	151/326 (36.2)		402/990 (40.6)	148/360 (41.1)	
71% to 90% stenosis	823/2,078 (39.6)	260/686 (37.9)		412/1,088 (37.9)	118/326 (36.2)		411/990 (41.5)	142/360 (39.4)	
91% to 99% stenosis	314/2,078 (15.1)	95/686 (13.8)		160/1,088 (14.7)	42/326 (12.9)		154/990 (15.6)	53/360 (14.7)	
Total occlusion	66/2,078 (3.2)	32/686 (4.7)		43/1,088 (4.0)	15/326 (4.6)		23/990 (2.3)	17/360 (4.7)	
Patients with									
Total occlusion	61 (8.2)	30 (11.5)	0.110	39 (10.2)	15 (12.0)	0.561	22 (6.1)	15 (11.0)	0.063
Proximal LAD lesion	297 (39.9)	99 (37.9)	0.572	159 (41.4)	51 (40.8)	0.905	138 (38.3)	48 (35.3)	0.533
Lesions segments 1, 2, 3, 6, 7, and 11	697 (93.7)	243 (93.1)	0.743	363 (94.5)	114 (91.2)	0.183	334 (92.8)	129 (94.9)	0.408
Quantitative coronary analysis									
Extent of stenosis, %	60.0 ± 16.6	60.6 ± 18.3	0.447	60.0 ± 17.2	60.0 ± 18.5	0.787	60.3 ± 15.9	61.2 ± 18.1	0.478
Minimal luminal diameter, mm	1.02 ± 0.44	0.98 ± 0.45	0.083	1.02 ± 0.45	1.02 ± 0.47	0.855	1.02 ± 0.43	0.95 ± 0.40	0.022
Reference diameter, mm	2.51 ± 0.63	2.41 ± 0.62	0.002	2.50 ± 0.64	2.46 ± 0.63	0.455	2.52 ± 0.62	2.37 ± 0.60	<0.001
Length of lesions per patient, mm	32.7 ± 18.0	27.9 ± 15.9	<0.001	33.4 ± 17.4	26.9 ± 15.2	<0.001	31.9 ± 18.6	28.9 ± 16.5	0.100
SYNTAX score	14.9 ± 9.2	13.4 ± 6.8	0.009	15.0 ± 9.1	13.1 ± 6.8	0.020	14.8 ± 9.4	13.7 ± 6.8	0.233
Procedural time, min	70 ± 42	70 ± 46	0.929	71 ± 40	70 ± 53	0.950	70 ± 45	70 ± 40	0.960
Volume of contrast agent used, ml	294 ± 134	268 ± 119	0.006	283 ± 137	241 ± 115	0.002	306 ± 131	293 ± 117	0.330
Total stented length per patient, mm	45.6 ± 27.2	42.6 ± 27.0	0.121	40.0 ± 27.7	31.7 ± 27.4	0.004	51.6 ± 25.4	52.6 ± 22.3	0.693
Implanted stents per patient, n	2.4 ± 1.2	2.3 ± 1.4	0.207	2.0 ± 1.2	1.6 ± 1.4	0.003	2.8 ± 1.1	2.9 ± 1.2	0.470

Values are mean ± SD or n (%).
LAD = left anterior descending artery; SYNTAX = Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery; other abbreviations as in Table 1.

comparable (78.8 ± 1.5% vs. 78.6 ± 2.6%, p = 0.820). Similarly, there were no significant sex-related differences in death-, MI-, and repeat revascularization–free survival. After adjustment for differences in baseline risk factors, 2-year MACE-free survivals were not different between men and women irrespective of the treatment method.

FFR values according to angiographic stenosis severity. In the FFR-guided group, a total of 1,414 lesions were noted in 509 patients. Of these, the FFR was measured successfully in 1,329 lesions (1,028 in men and 301 in women) (11). The lesions were categorized into 50% to 70%, 71% to 90%, and 91% to 99% diameter stenosis by visual estimation. Angiographic lesion severity per category and its respective FFR values are presented in Figure 1. FFR values were significantly higher in women than in men (0.75 ± 0.18 vs. 0.71 ± 0.17, p = 0.001). The proportion of functionally significant lesions (FFR ≤0.80) was lower in women than in men for lesions with 50% to 70% stenosis (21.1% vs. 39.5%, p < 0.001) and for lesions with 70% to 90% stenosis (71.9% vs. 82.0%, p = 0.019). In the 91% to 99% category, the proportion of patients

Table 3. MACE Between Men and Women

	Total: Men (n = 744)	Total: Women (n = 261)	Total: p Value	FFR-Guided PCI: Men (n = 384)	FFR-Guided PCI: Women (n = 125)	FFR-Guided PCI: p Value	Angiography-Guided PCI: Men (n = 360)	Angiography-Guided PCI: Women (n = 136)	Angiography-Guided PCI: p Value
Composite of MACE	149 (20.2)	53 (20.3)	0.923	67 (17.4)	24 (19.2)	0.657	82 (22.8)	29 (21.3)	0.729
Death	25 (3.4)	7 (2.7)	0.591	10 (2.6)	3 (2.4)	0.900	15 (4.2)	4 (2.9)	0.526
MI	60 (8.1)	20 (7.7)	0.837	23 (6.0)	8 (6.4)	0.868	37 (10.3)	12 (8.8)	0.628
Repeat revascularization	85 (11.4)	32 (12.3)	0.717	40 (10.4)	14 (11.2)	0.805	45 (12.5)	18 (13.2)	0.826
Death or MI	81 (10.9)	26 (10.0)	0.677	32 (8.3)	11 (8.8)	0.871	49 (13.6)	15 (11.0)	0.444

Values are n (%).
MACE = major adverse cardiac events; other abbreviations as in Table 1.

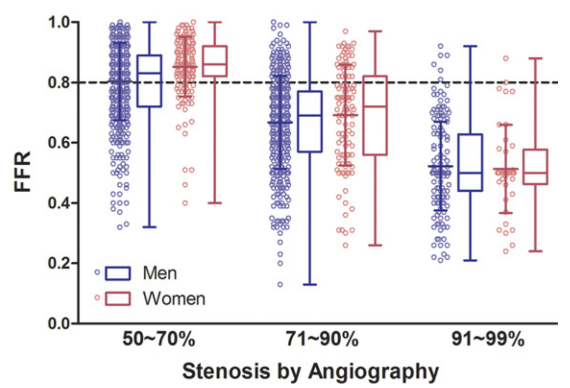

Figure 1. FFR Values According to Angiographic Stenosis Severity

FFR = fractional flow reserve.

with FFR ≤0.80 was not different between women and men (97.5% vs. 96.2%, p = 0.682).

Similarly, the proportion of functionally significant lesions was significantly lower in women than in men with stenosis in the 50% to 90% range measured by quantitative coronary analysis: for 50% to 70% stenosis (54.5% vs. 65.2%, p = 0.032) and for 70% to 90% stenosis (77.6% vs. 89.6%, p = 0.017).

Risk reduction with FFR-guidance. During the 2-year follow-up, MACE occurred in 17.4% in the FFR-guided group and in 22.8% in the angiography-guided group for men and in 19.2% and in 21.3%, respectively, for women. The death, MI, and repeat revascularization rates were 2.6%, 6.0%, and 10.4%, respectively, in FFR-guided group versus 4.2%, 10.3%, and 12.5%, respectively, in angiography-guided group for men and 2.4%, 6.4%, and 11.2% versus 2.9%, 8.8%, and 13.2% for women. The 2-year survivals free from MACE are depicted in Figure 2.

The relative risk reductions for death, MI, and repeat revascularization of FFR relative to angiography-guided treatment were 37%, 42%, and 17%, respectively, in men and 18%, 27%, and 15%, respectively, in women. Treatment method-by-sex interaction tests were not statistically significant for any of the outcome variables (p > 0.05).

Discussion

The 3 main findings of this study are: 1) the proportion of functionally significant lesions (FFR ≤0.80) is lower in women than in men with coronary stenoses between 50% and 90% narrowed; 2) an FFR-guided PCI strategy is equally beneficial in women as it is in men; and 3) although women in this study were older and tended to have higher rates of baseline comorbidities, their 2-year rates of cardiac events are similar to those in men irrespective of treatment strategy (FFR- or angiography-guided therapy).

FFR, a lesion-specific index, is superior to noninvasive modalities for assessing the ischemic propensity of individual coronary lesions (12). Although it has been increasingly used to guide clinical decision making in several patient and lesion subsets (8,13–15), the differences in FFR results in women and men have not been previously evaluated. We demonstrated significantly higher FFR values in women than in men, despite a similar degree of angiographic stenosis and minimal luminal diameter. The proportion of functionally significant lesions (FFR ≤0.80) was significantly lower in women than in men for lesions with 50% to 90% stenosis, which suggests that lesions of similar angiographic severity are less likely to be ischemia-producing in women.

Higher FFR for similar angiographic stenosis in women may be a chance finding. However, a potential explanation for this finding is that in this study and others, women were older and more likely to have hypertension and left ventricular hypertrophy. One would expect them to have a greater degree of diastolic dysfunction, although this was not specifically studied. These abnormalities could result in microvascular dysfunction (16), less hyperemia, and lower peak flow across any given stenosis, manifesting as a higher FFR. It could also possibly be explained by the fact that because women generally have smaller myocardial mass (17), a smaller myocardial perfusion territory will be subtended by a stenosed vessel (18) and the flow across any given stenosis may be less (19), thereby requiring a more severe stenosis to be functionally significant. The higher FFR values in women in this study might also be due to the visual estimation of stenosis severity, which has been previously shown to be more variable and inaccurate in women, presumably due to vessel size (20,21).

We found no interaction between sex and the benefits of FFR-guided PCI over angiography-guided PCI on 2-year rates of MACE. As this was a post-hoc subset analysis and the number of patients in each subgroup was below the statistical power needed for significance, caution is required

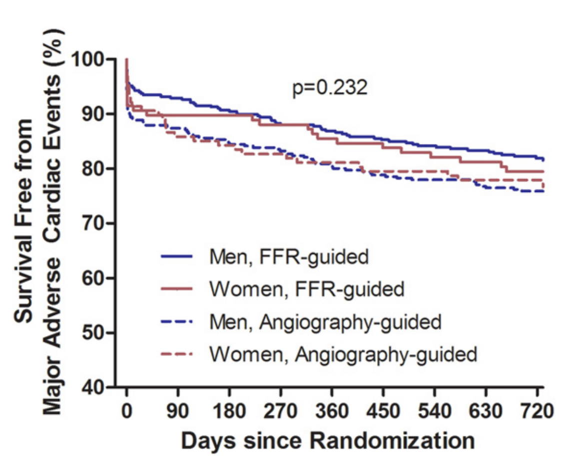

Figure 2. Kaplan-Meier Curves of Freedom From MACE

FFR = fractional flow reserve; MACE = major adverse cardiac events.

in interpreting these results. However, there was no heterogeneity in benefit of FFR guidance among the subgroups for any of the outcome variables (p values were all >0.05). Our study suggests that FFR-guided therapy is superior to angiography-guided therapy in reducing adverse clinical events after multivessel PCI, regardless of sex.

The final finding in this study is that the results of PCI in women, whether guided by FFR or angiography were equivalent to those in men. Older studies have shown that women have worse outcomes compared with men undergoing PCI (1,2). More contemporary studies incorporating modern medical therapy and use of DES have shown no difference in outcomes between sex (3–5). The results of the current study, which incorporates modern medical therapy and DES, found similar 2-year rates of cardiac events in men and women.

Study limitations. The main limitations of this study include that it was a post hoc subanalysis of patients in the FAME study and therefore the findings should only be hypothesis generating. Because a relatively small number of women were included, the subanalysis is underpowered to determine whether FFR-guided therapy is superior to angiography-guided therapy in women with multivessel disease. Although caution is required in generalizing our findings to all patients with multivessel disease, this study was the first, to our knowledge, to evaluate the effect of sex differences on FFR-guided therapy for multivessel coronary intervention.

Conclusions

The clinical implications of this study are important. Because women appear to have higher FFR values for a given stenosis, it may be even more relevant to measure FFR in women to confirm hemodynamic significance before performing PCI.

In conclusion, angiographic lesions of similar severity are less likely to be ischemia-producing in women as compared to men and an FFR-guided PCI strategy in patients with multivessel disease is equally beneficial in women as it is in men.

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Key Words: fractional flow reserve ■ multivessel disease ■ sex difference.