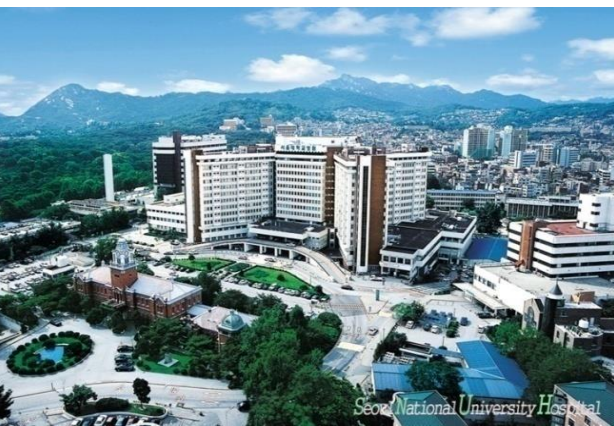


Sex Differences in Plaque Characteristics and Myocardial Mass : Implications for Physiologic Significance

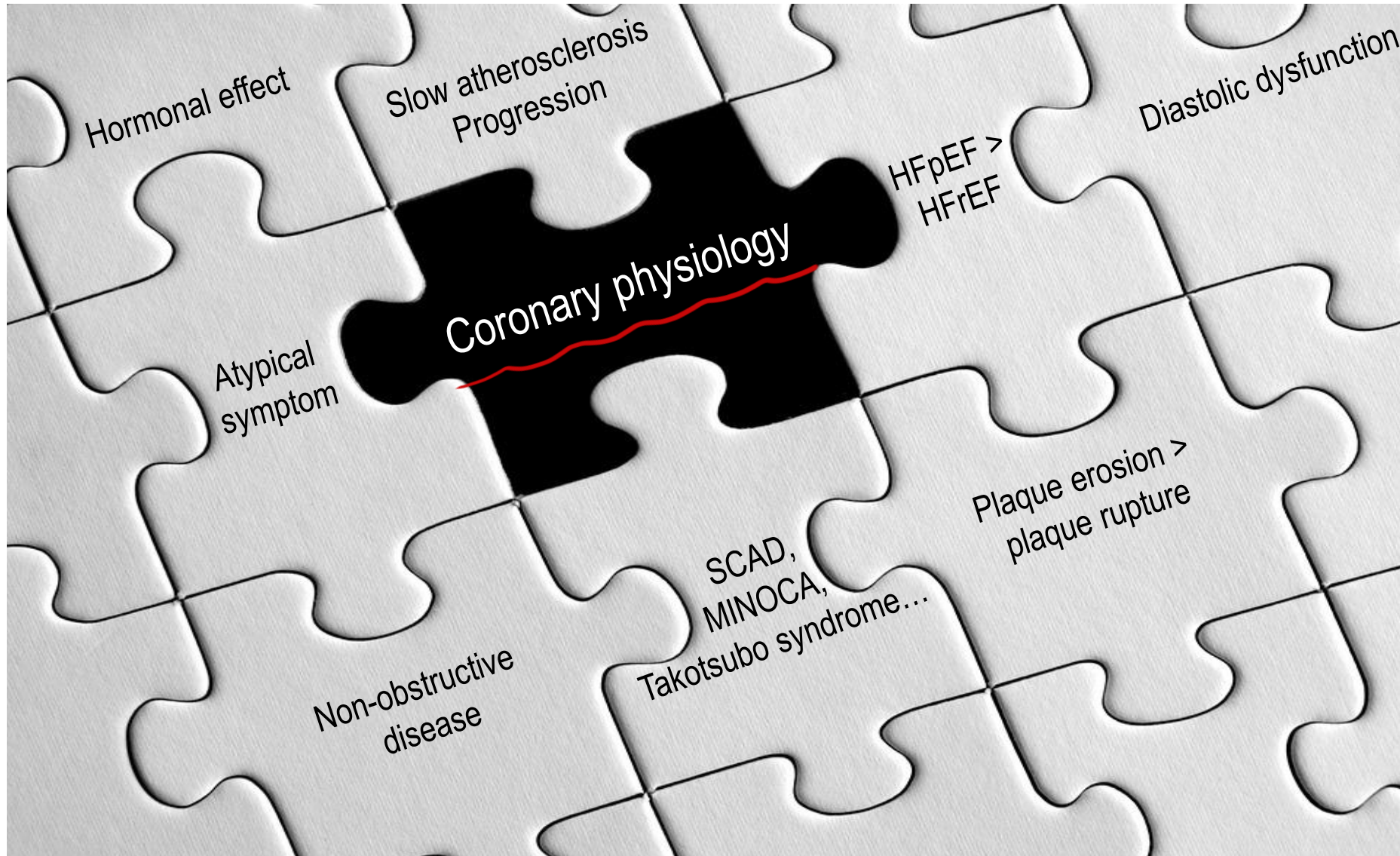
Bon-Kwon Koo, MD, PhD/Chee Hae Kim MD*

Seoul National University Hospital, Seoul, Korea

*VHS Medical Center, Seoul, Korea



Understanding Coronary Artery Disease in Women

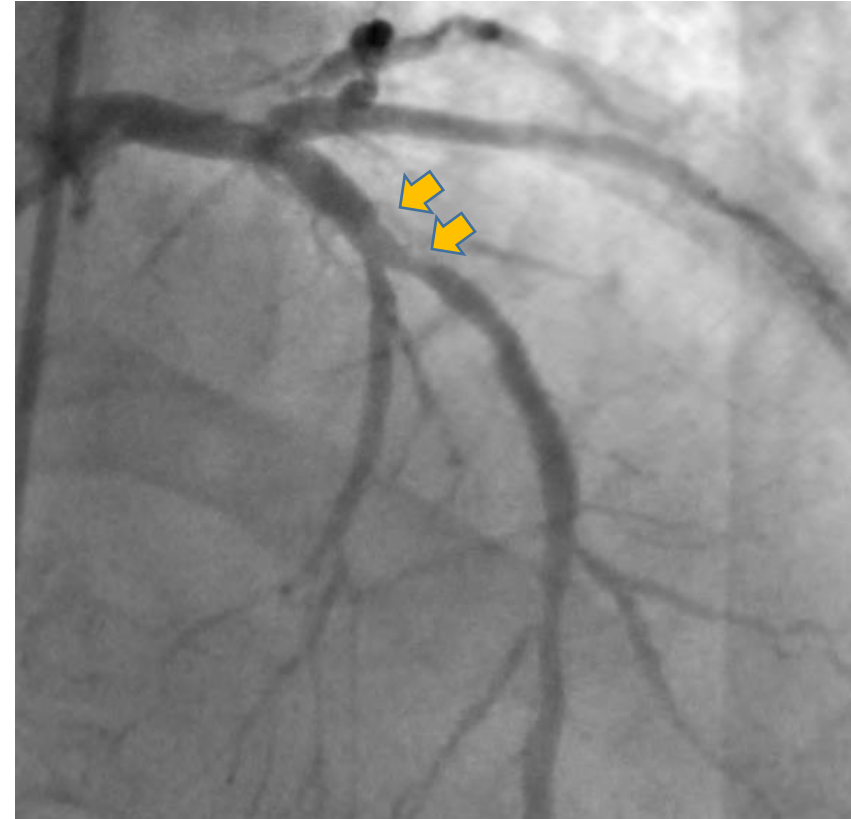


Significant stenosis?

FEMALE Stable Angina, HTN/DM (+/-)



MALE Stable Angina, HTN/DM (+/+)

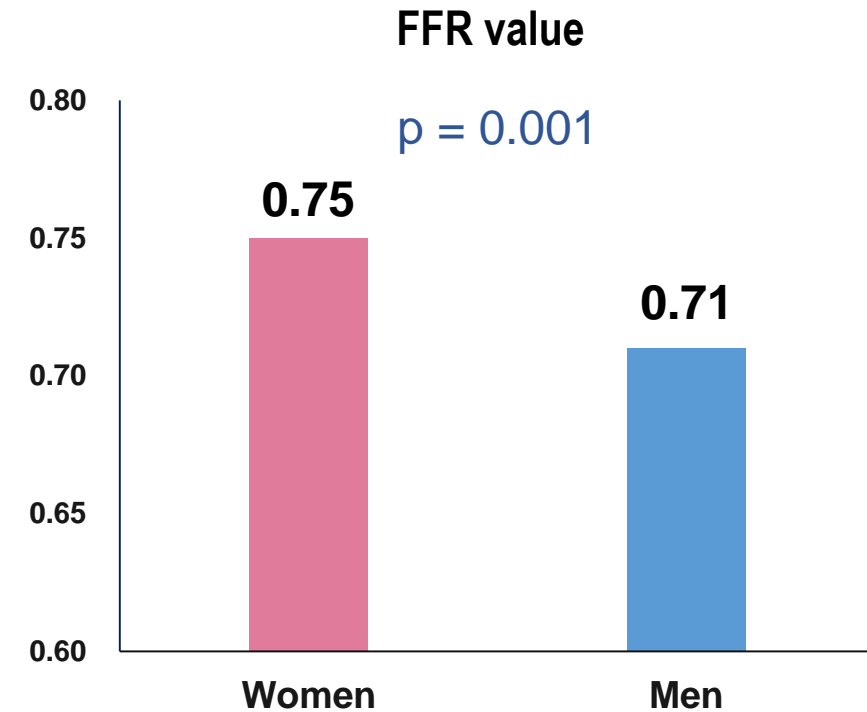


FAME Study Sex Issue

FFR in Women

1,005 Patients with Multi-vessel Coronary Artery Disease

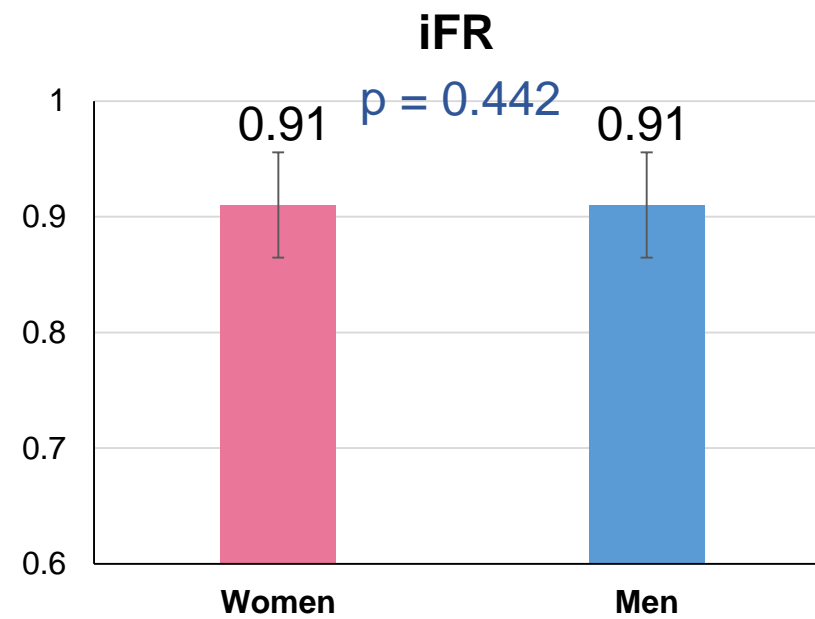
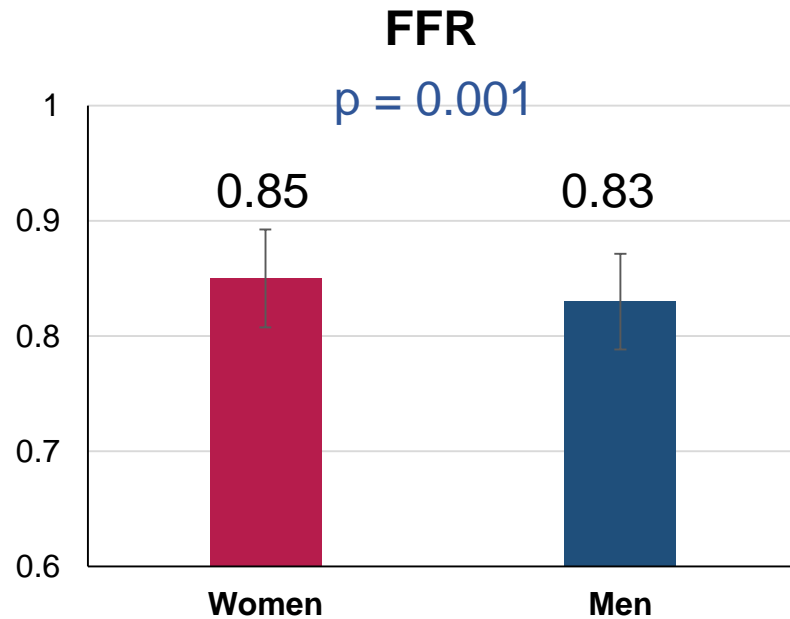
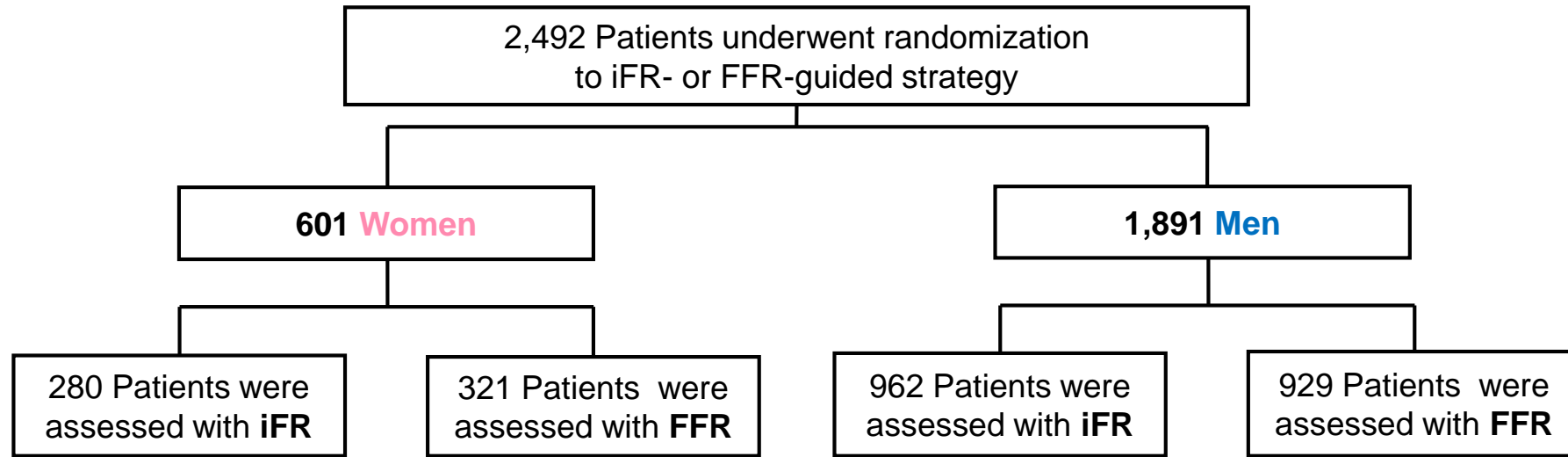
	Women (n=261)	Men (n=744)	P
Age, years	68.3 ± 9.5	63.1 ± 10.2	<0.001
Hypertension	188 (72%)	451 (61%)	0.001
Diabetes mellitus	69 (26%)	528 (71%)	0.102
QCA			
Diameter stenosis, %	60.6 ± 18.3	60.0 ± 16.6	0.447
Minimal luminal diameter, mm	0.98 ± 0.45	1.02 ± 0.44	0.083
Reference diameter, mm	2.41 ± 0.62	2.51 ± 0.63	0.002



Mean FFR value was higher in women for the same stenosis severity

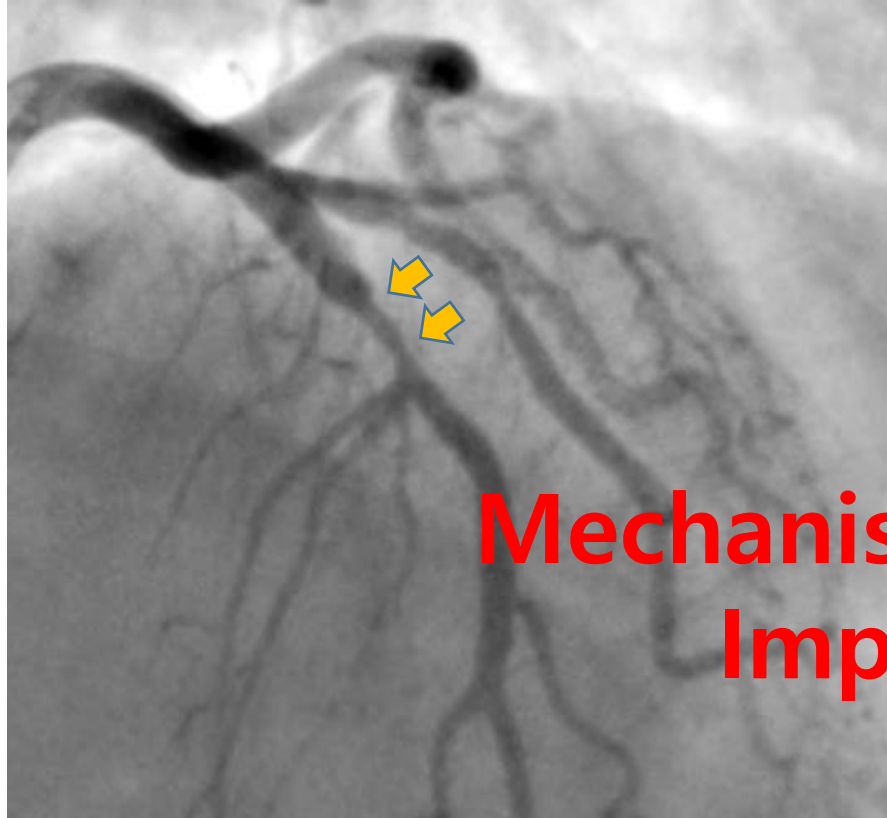
Sex Difference in Physiologic Indexes

DEFINE FLAIR



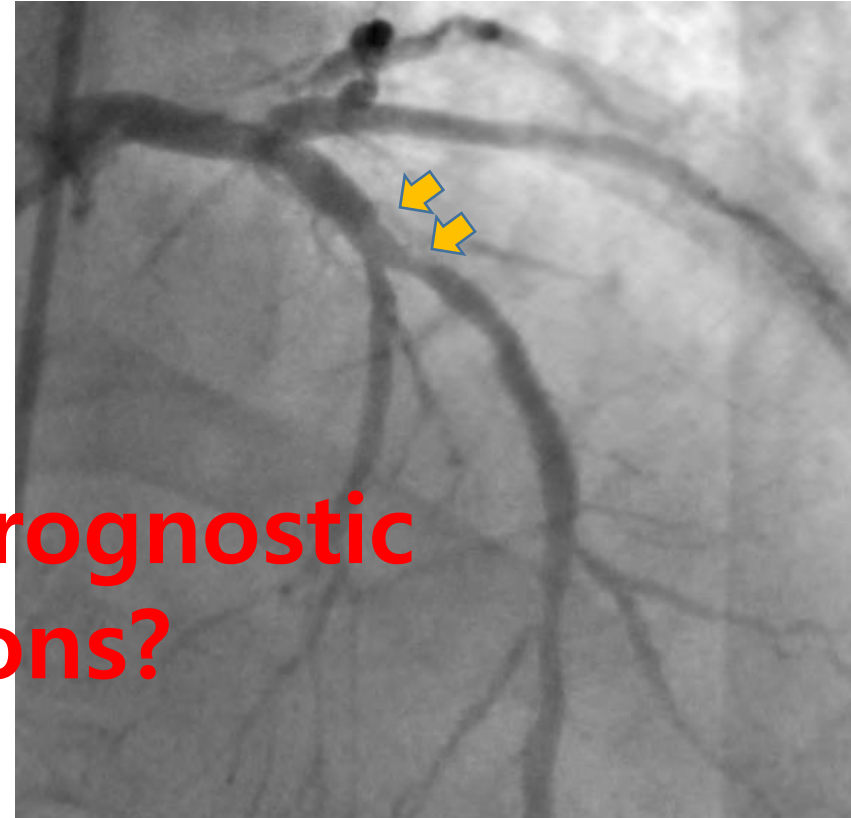
Significant stenosis?

FEMALE Stable Angina, HTN/DM (+/-)



FFR 0.85 → Medical Tx

MALE Stable Angina, HTN/DM (+/+)



FFR 0.76 → PCI

Mechanism? Prognostic Implications?

Sex Differences in Plaque Characteristics and Myocardial Mass

: Implications for Physiologic Significance

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¹ Department of Internal Medicine and Cardiovascular Center, Dongguk University Ilsan Hospital, Goyang, Korea; ² Department of Internal Medicine and Cardiovascular Center, Seoul National University, Seoul, Korea;

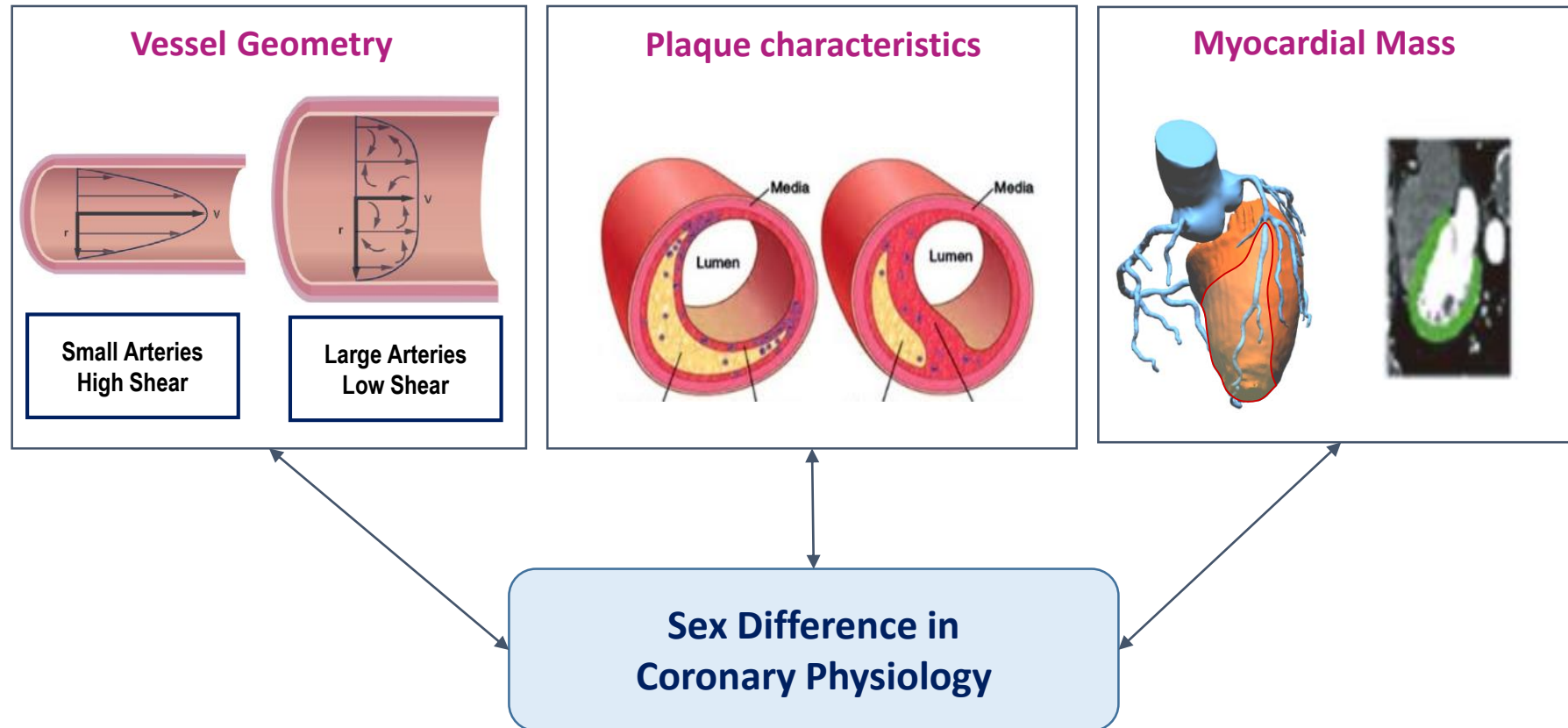
³ Department of Cardiology, The Second Affiliated Hospital, School of Medicine, Zhejiang University, Hangzhou, China; ⁴ Division of Cardiology, Department of Internal Medicine, Heart Vascular Stroke Institute, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea; ⁵ Division of Cardiovascular Medicine, Tsuchiura Kyodo General Hospital, Ibaraki, Japan; ⁶ Division of Cardiology, Ulsan Hospital, Ulsan, Korea; ⁷ Department of Medicine, Department of Medicine, Inje University Ilsan Paik Hospital, Goyang, Korea; ⁸ Department of Medicine, Keimyung University Dongsan Medical Center, Daegu, South Korea; ⁹

Department of Cardiology, The Second Affiliated Hospital, School of Medicine, Zhejiang University, China; ¹⁰ Department of Cardiology, Nanjing First Hospital, Nanjing Medical University, Nanjing, China; ¹¹ Department

of Cardiology, Tokyo Medical University, Tokyo, Japan; ¹² Department of Cardiology, Gifu Heart Center, Gifu, Japan; ¹³ Wakayama Medical University, Wakayama, Japan; ¹⁴ Institute on Aging, Seoul National University, Seoul, Korea

Hypothesis and Aim

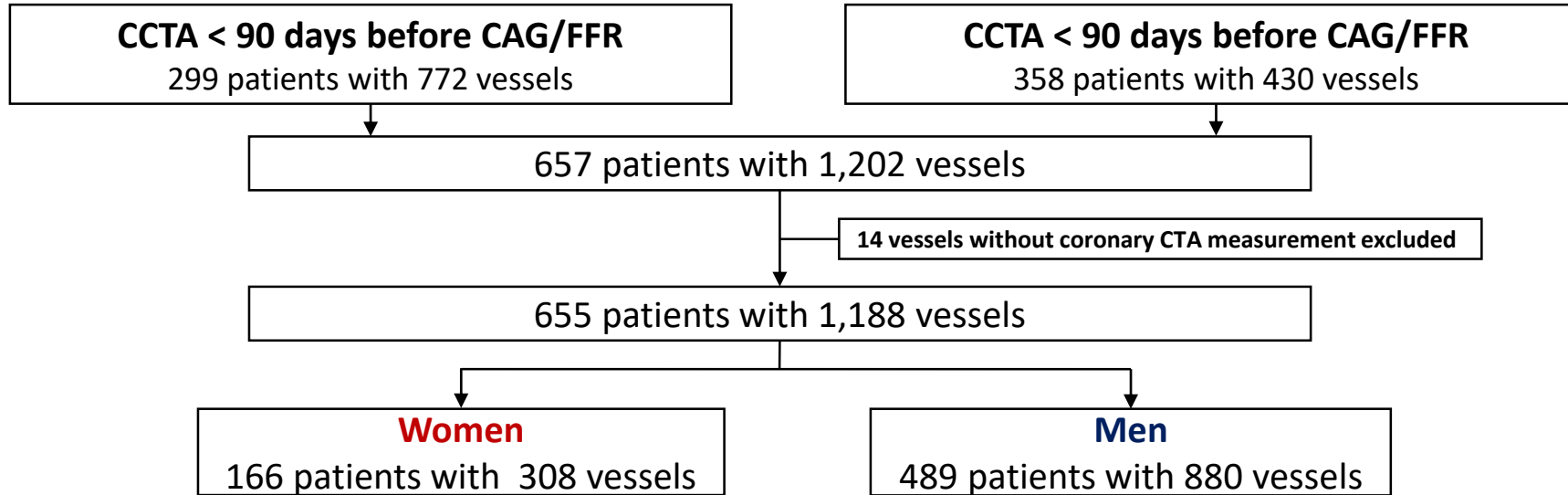
To evaluate sex differences in plaque characteristics and myocardial mass and their implications for physiologic significance and clinical outcome



Study Population and Measurements

3V FFR-FRIENDS study

Institutional registry of Tsuchiura Kyodo General Hospital



Core Laboratory CCTA measurements

- **LV mass**
- **2D cross-sectional analysis** – minimal lumen area (MLA), % plaque burden
- **3D whole vessel analysis** – vessel/plaque/lumen volume, % mean plaque burden
- **Plaque composition** – fibrous plaque/fibrofatty plaque/necrotic core/calcified plaque
- **Quantitative plaque characteristics** – FFNC (fibrofatty + necrotic core) volume, %FFNC volume
- **Qualitative plaque characteristics** – low-attenuation plaque/positive remodeling/napkin-ring sign/spotty calcification

**Invasive coronary angiography
FFR measurements**

VOCO at 5 years in deferred vessels
(cardiac death, vessel-related MI, vessel-related revascularization)

Baseline Characteristics

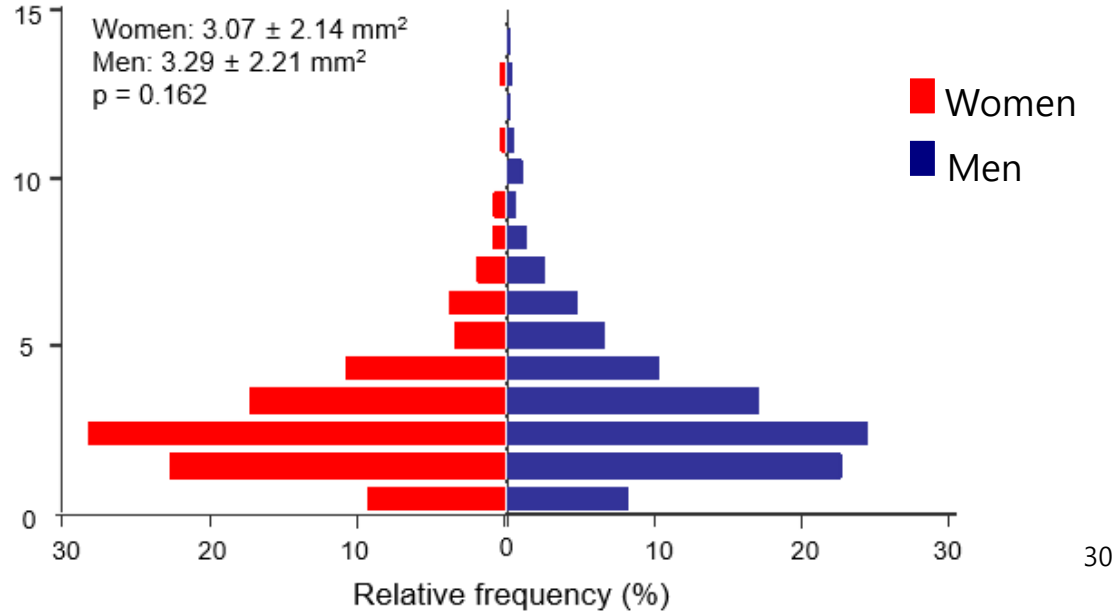
	Women	Men	p
<i>Patient characteristics</i>	(n = 166)	(n = 489)	
Age, years	69.8 ± 9.4	64.8 ± 9.9	<0.001
Hypertension	127 (76.5%)	324 (66.3%)	0.014
Diabetes mellitus	56 (33.7%)	174 (35.6%)	0.666
Hypercholesterolemia	98 (59.0%)	275 (56.2%)	0.529
Acute coronary syndrome	33 (19.9%)	92 (18.8%)	0.763
<i>Lesion characteristics</i>	(n = 308)	(n = 880)	
Lesion location			0.633
Left anterior descending artery	144 (46.8%)	418 (47.5%)	
Left circumflex artery	85 (27.6%)	220 (25.0%)	
Right coronary artery	79 (25.6%)	242 (27.5%)	
Quantitative coronary angiography			
Reference vessel diameter, mm	2.81 ± 0.59	2.96 ± 0.64	<0.001
Minimal lumen diameter, mm	1.54 ± 0.66	1.62 ± 0.68	0.077
% Diameter stenosis, %	45.9 ± 18.9	46.1 ± 17.7	0.920
Lesion length, mm	11.8 ± 9.5	12.3 ± 9.2	0.430
FFR	0.85 ± 0.13	0.82 ± 0.14	0.001
FFR ≤ 0.80	90 (29.2%)	355 (40.3%)	0.001

CCTA Characteristics

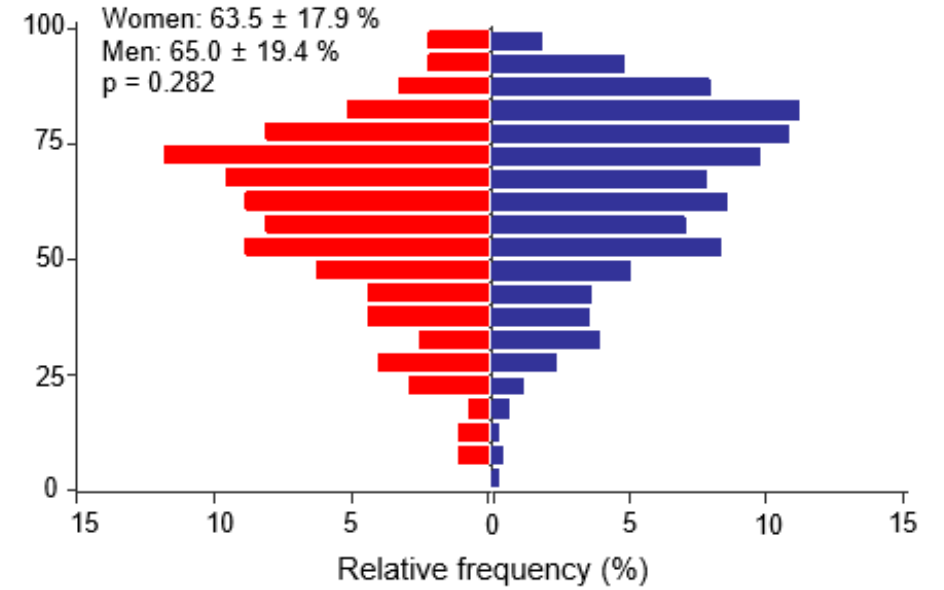
	Women	Men	p
LV mass, g	102.4 ± 27.4	128.9 ± 34.4	<0.001
2D Cross-sectional analysis at MLA site			
Vessel wall area, mm ²	8.89 ± 4.54	10.25 ± 5.02	<0.001
MLA, mm ²	3.07 ± 2.14	3.29 ± 2.21	0.162
% Plaque burden, %	63.5 ± 17.9	65.0 ± 19.4	0.282
3D Whole vessel analysis			
Vessel length, mm	93.9 ± 38.5	107.5 ± 39.5	<0.001
Vessel volume, mm ³	631.8 ± 337.7	778.1 ± 407.1	<0.001
Plaque volume, mm ³	146.4 ± 119.7	195.3 ± 171.9	<0.001
Lumen volume, mm ³	508.2 ± 282.1	609.2 ± 334.5	<0.001
% Mean plaque burden, %	22.3 ± 13.8	23.5 ± 14.8	0.246
Fibraofatty + necrotic core volume, mm ³	19.3 ± 30.3	45.7 ± 64.3	<0.001
% Fibrofatty + necrotic core volume, %	13.1 ± 16.9	21.2 ± 19.9	<0.001

Distributions of CCTA parameters

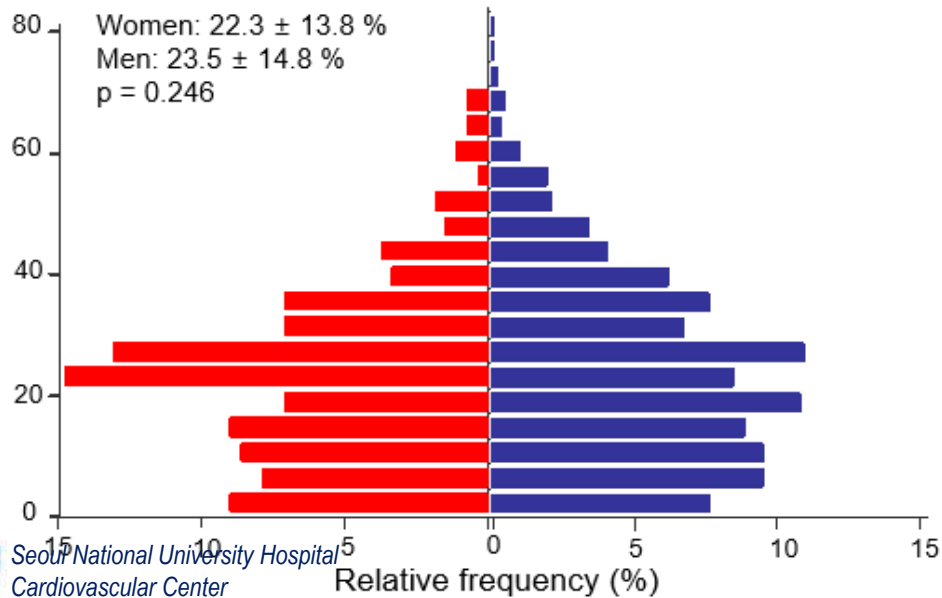
(A) MLA



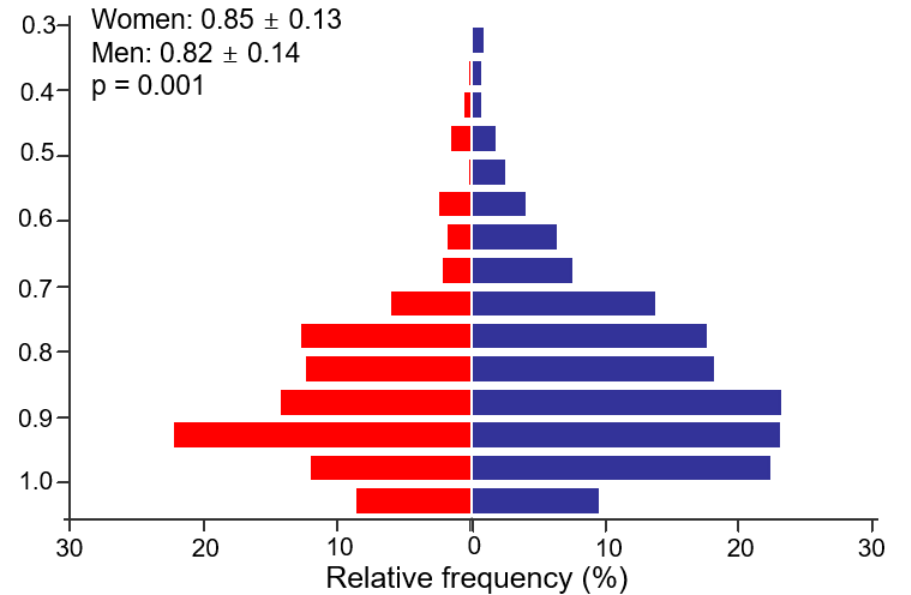
(B) % Plaque burden at MLA site



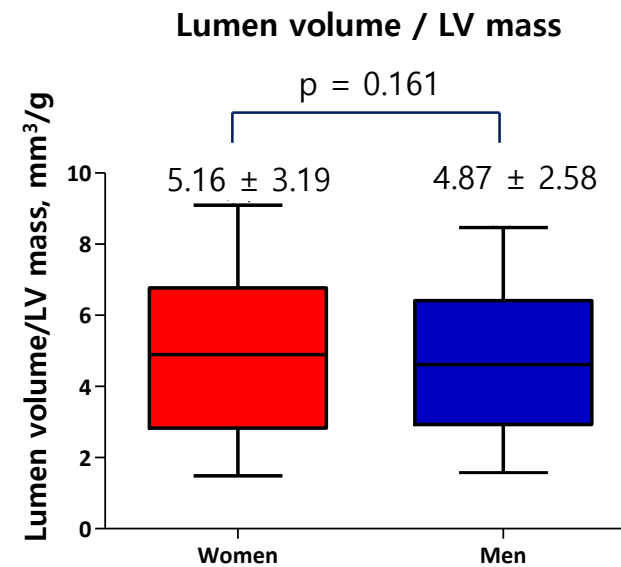
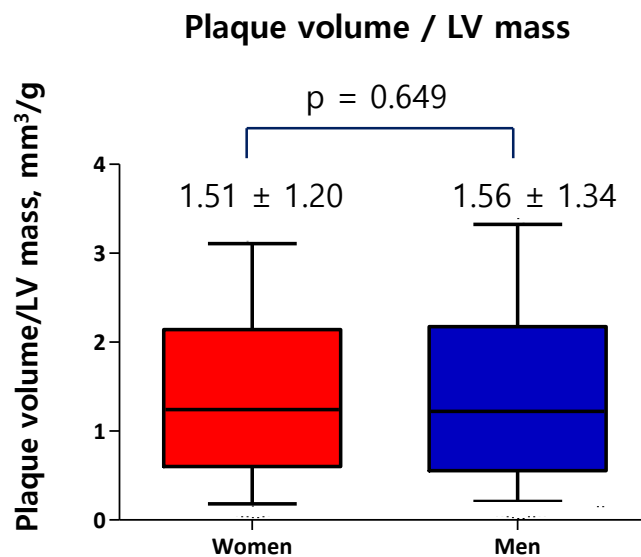
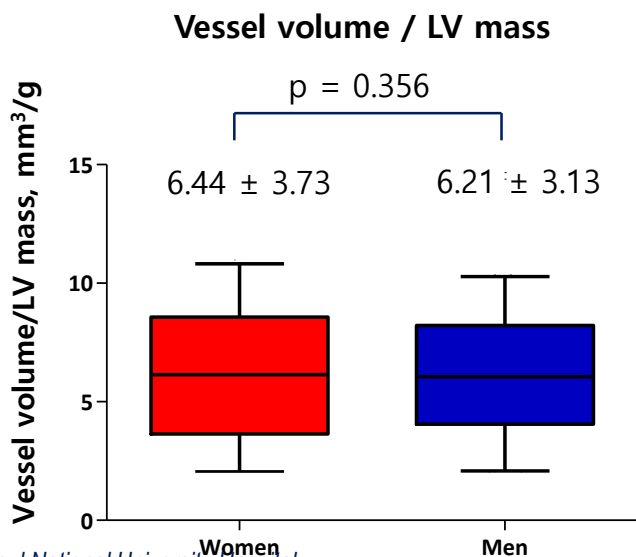
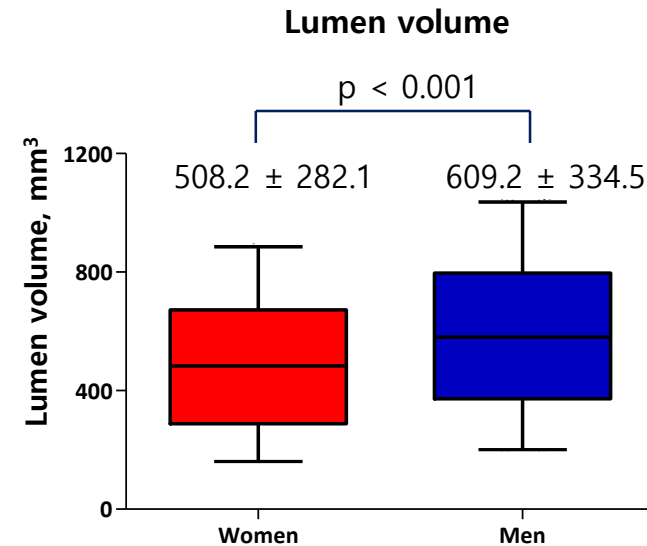
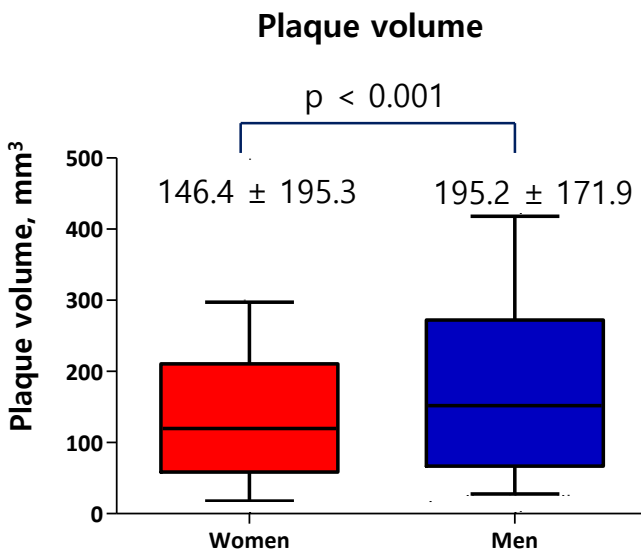
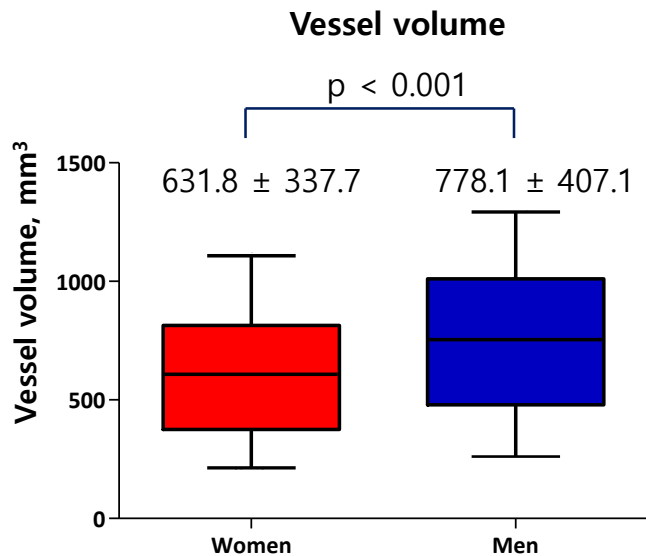
(3) % Mean plaque burden



(4) FFR

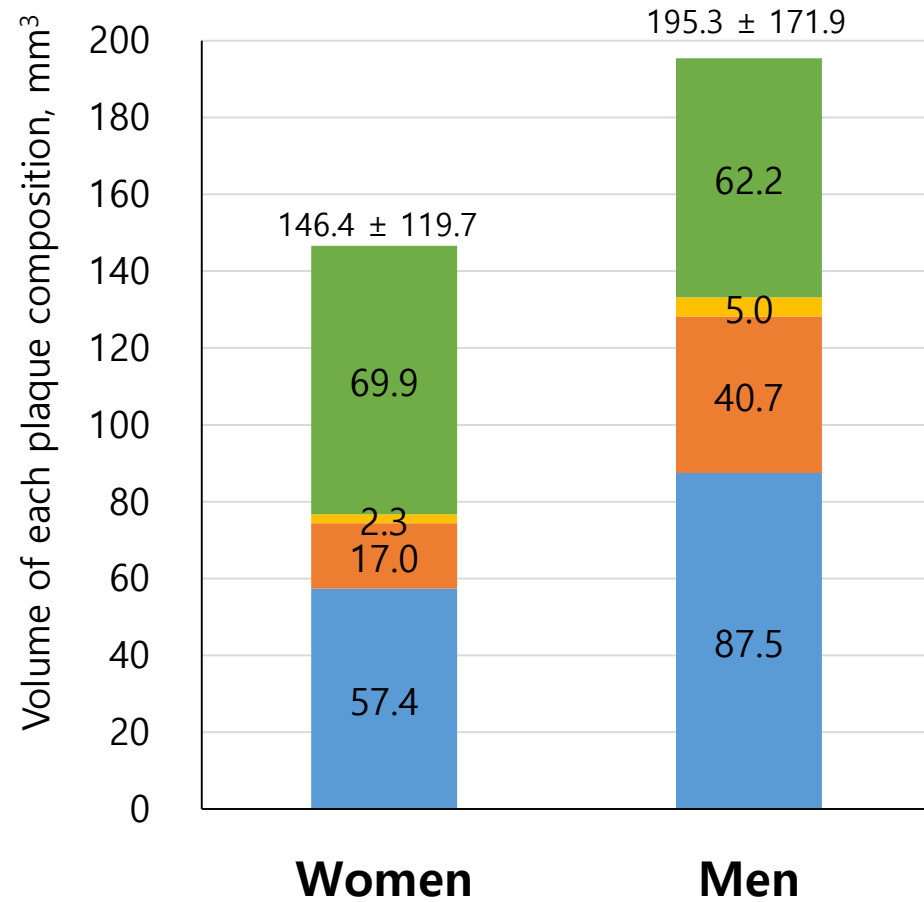


Vessel, plaque, and lumen volume according to sex before and after adjustment for LV mass

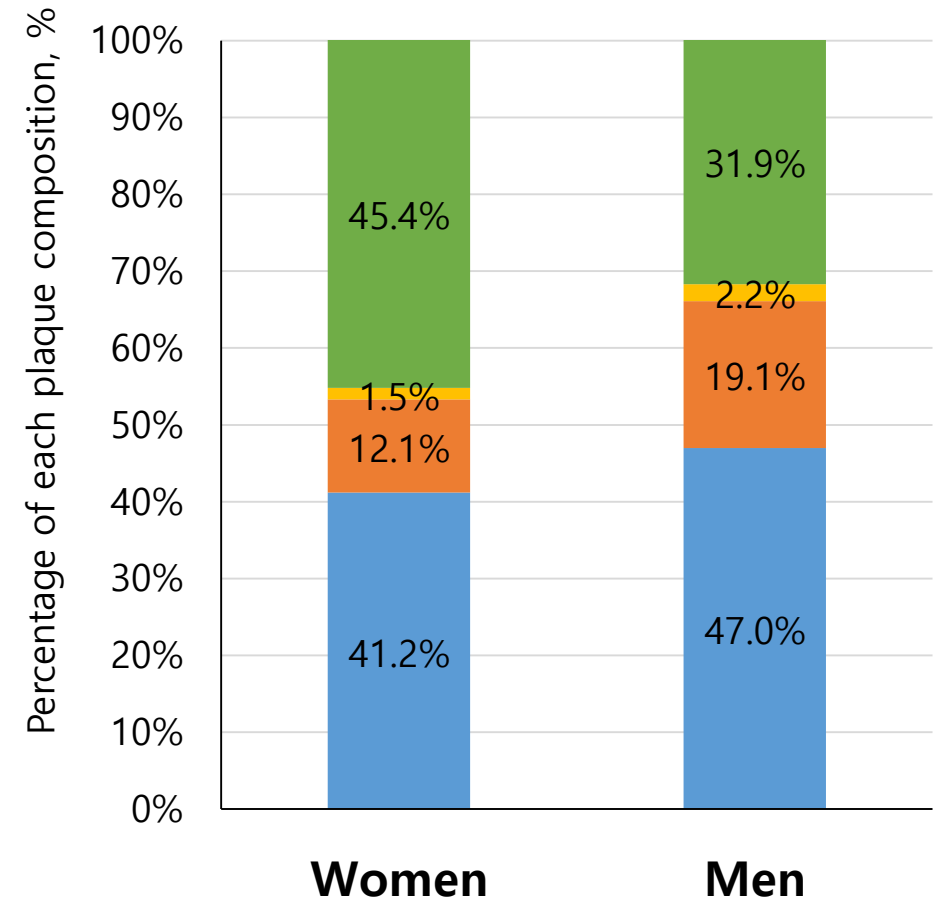


Plaque composition according to sex

Volume of each plaque composition

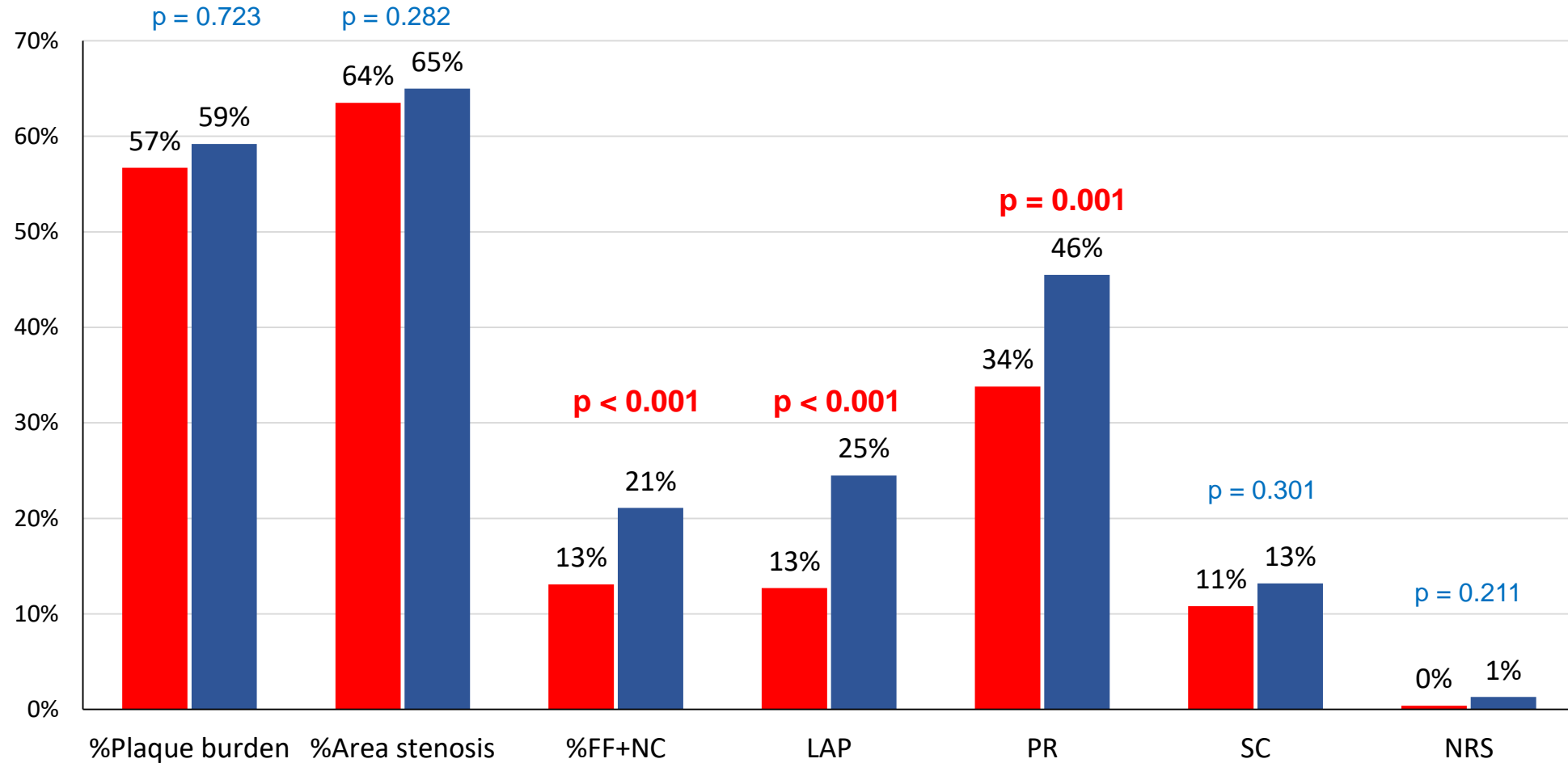


Percentage of each plaque composition



- Dense calcium
- Necrotic core
- Fibrofatty plaque
- Fibrous plaque

Quantitative and Qualitative Plaque Characteristics



Independent Predictors of FFR

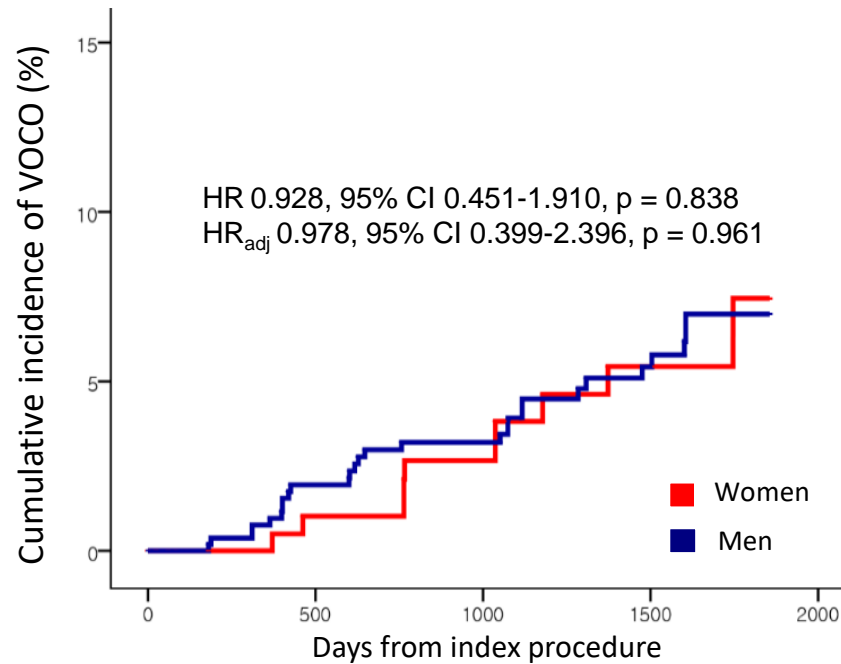
* Adjusted for stenosis severity, age, acute coronary syndrome, and vessel location.

	Variables	B	Beta	p
Model 1	Sex (Women)	0.028	0.090	0.001
Model 2	Sex (Women)	0.020	0.065	0.025
	LV mass	0.000	-0.108	<0.001
Model 3	Sex (Women)	0.020	0.063	0.018
	Low attenuation plaque	-0.029	-0.088	0.001
	Positive remodeling	-0.022	-0.080	0.005
	Fibrofatty + necrotic core volume	0.000	-0.090	0.003
Model 4	Sex (Women)	0.013	0.040	0.170
	LV mass	0.000	-0.096	0.001
	Low attenuation plaque	-0.026	-0.079	0.005
	Positive remodeling	-0.024	-0.085	0.003
	Fibrofatty + necrotic core volume	0.000	0.099	0.002

Clinical Outcome in Deferred Vessels (458 patients with 803 vessels)

VOCO at 5 years

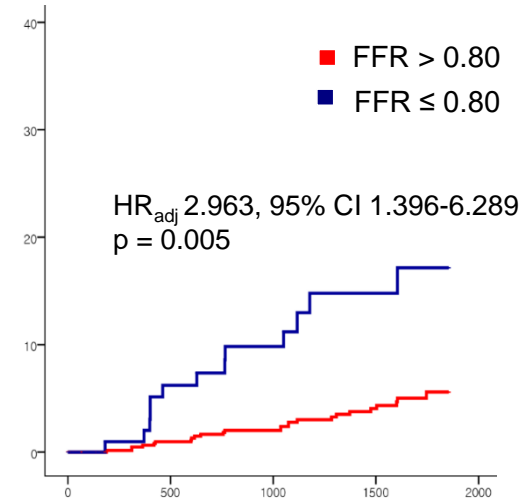
Women vs. Men



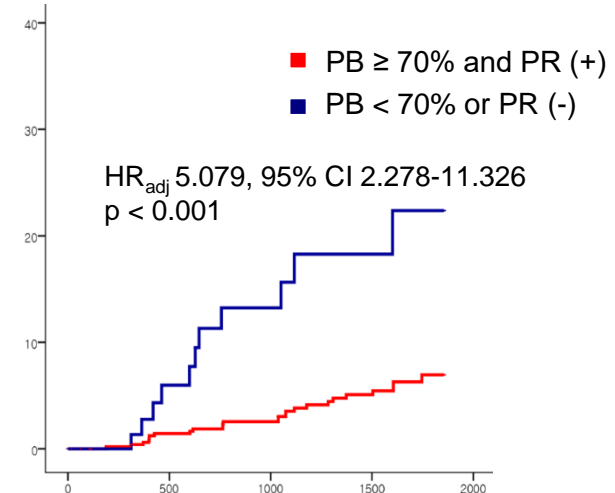
No. at risk

Men	568	491	441	276
Women	235	195	177	103

FFR



Plaque Characteristics

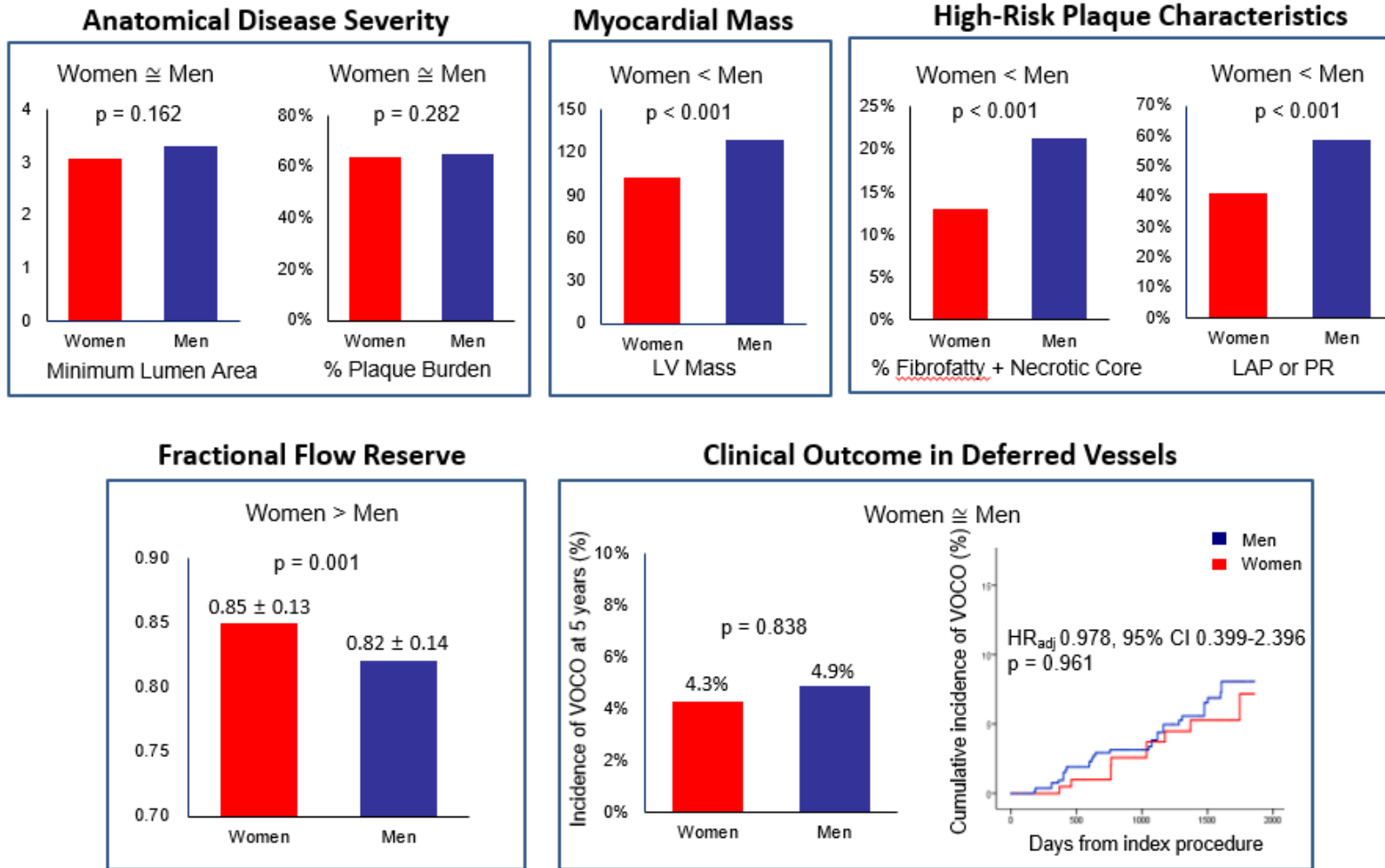


Clinical Outcome in Deferred Vessels

Determinants of 5-year VOCCO

	HR _{adj}	95% CI	p
Diabetes mellitus	4.719	2.259-9.859	<0.001
FFR ≤ 0.80	2.963	1.396-6.289	0.005
Positive remodeling	2.673	1.310-5.455	0.007
% Plaque burden ≥ 70%	2.313	1.036-5.166	0.041
Sex (women)	0.978	0.399-2.396	0.961
Acute coronary syndrome	1.529	0.673-3.473	0.311
Low attenuation plaque	1.309	0.538-3.187	0.552
MLA ≤ 4 mm ²	1.130	0.458-2.786	0.791
Hypertension	1.034	0.465-2.298	0.935
Age	1.000	0.963-1.039	0.985
LV mass	1.000	0.987-1.012	0.970
Ibuprofen + necrotic core volume	0.996	0.986-1.007	0.479

Summary and Conclusion



- Higher FFR value for the same stenosis severity in women can be explained by a **smaller myocardial mass** and **less high-risk plaque characteristics** than in men.
- Among deferred vessels, sex was not an independent predictor for clinical outcome.