Is There (real) Gender Difference in Prognosis of Ischemic Heart Disease?

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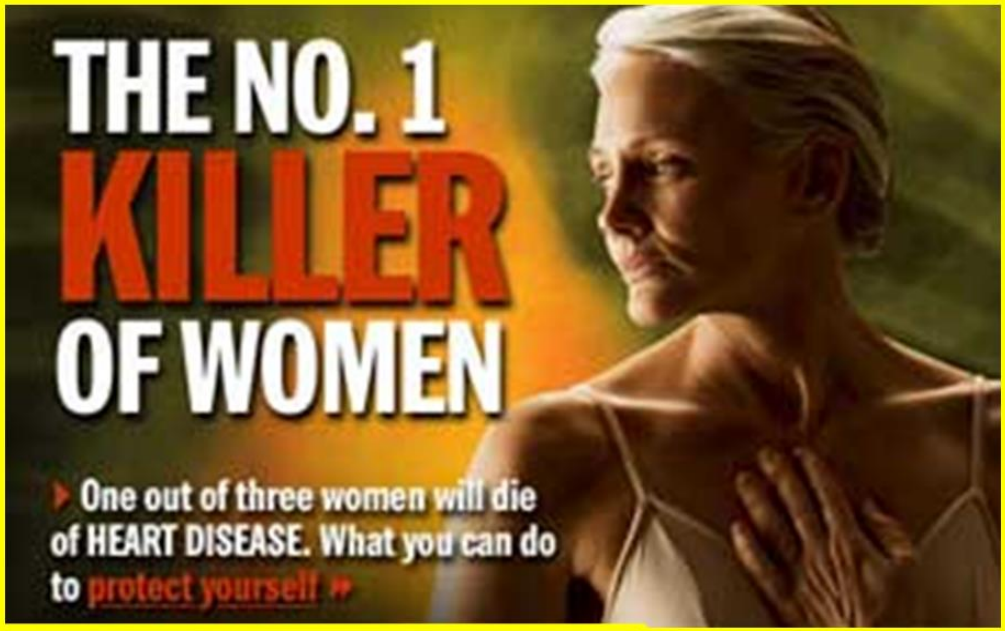
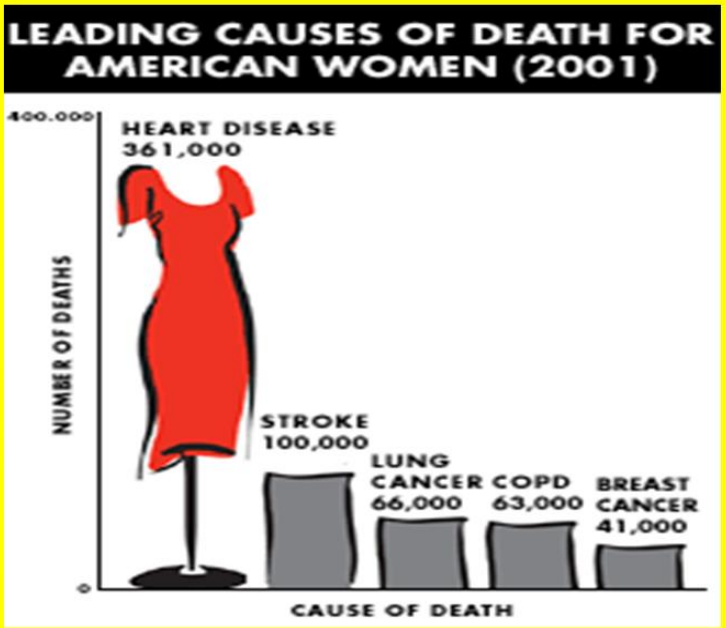
안영근

Underestimated ischemic heart disease in women





What women think they will die of :

BREAST CANCER	40-60%
Heart Disease	15-18%

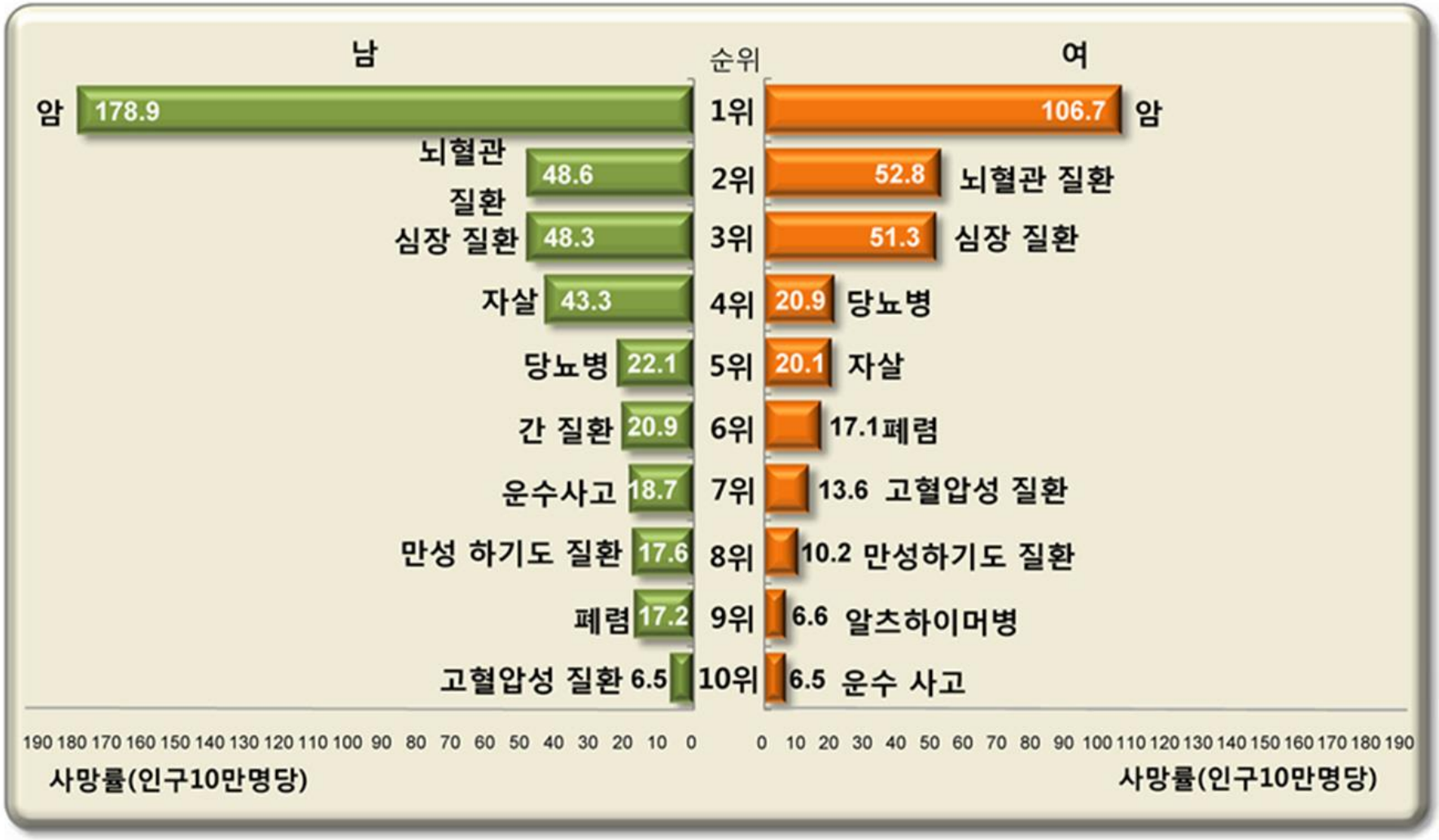
What women ACTUALLY die from:

CARDIOVASCULAR DISEASE	53%
Breast Cancer	4%

Go Red for women

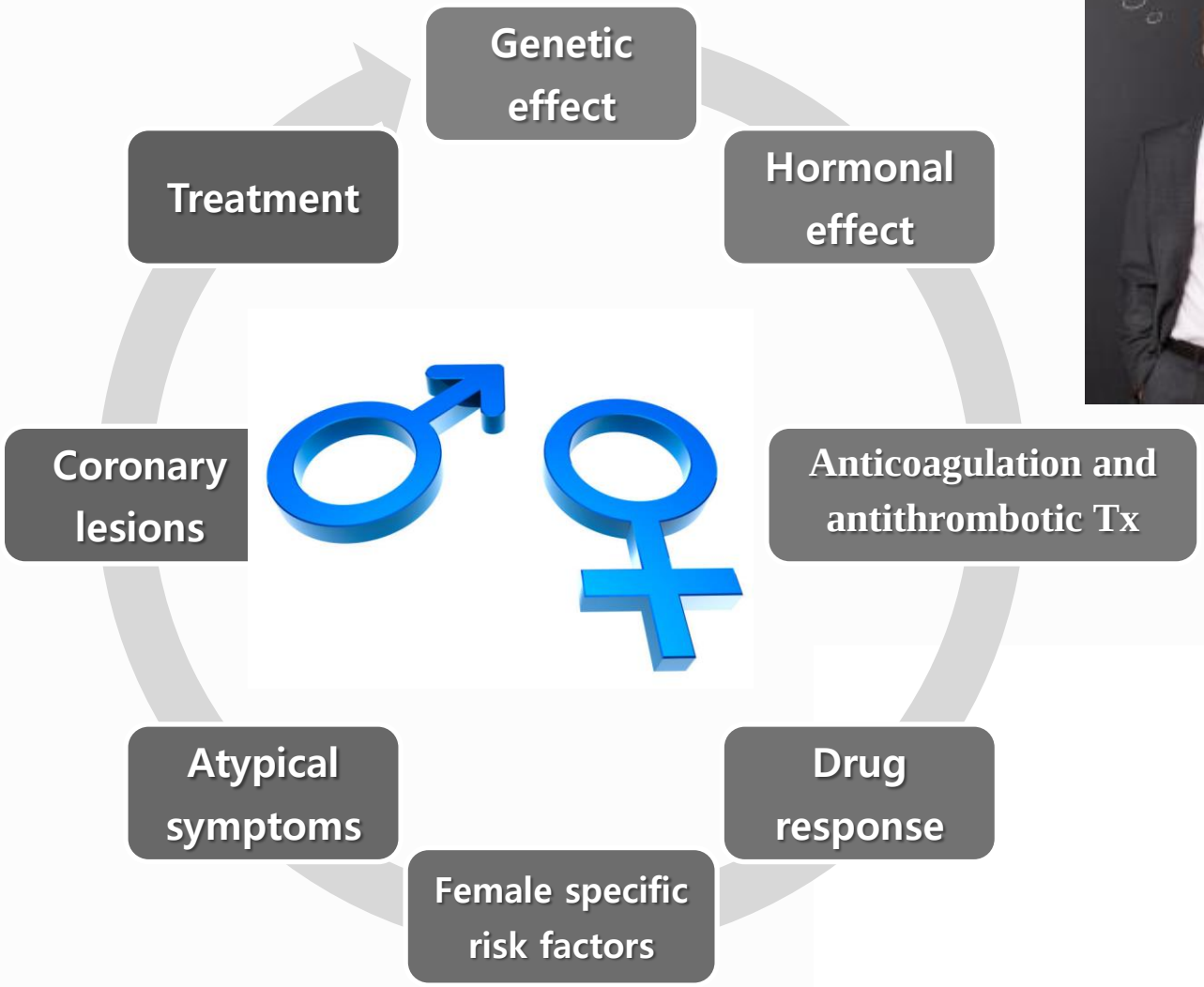
Americans nationwide will take women's health to heart by wearing red to show their support for women's heart disease awareness

2011 대한민국 사망원인통계



통계청 '2011 사망원인통계'

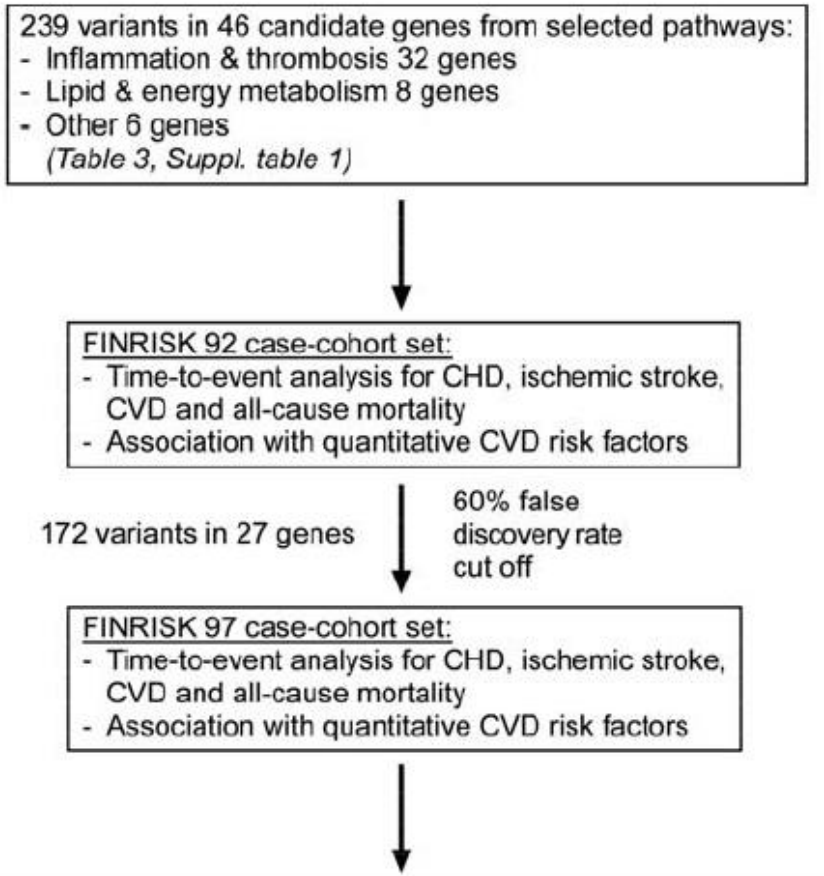
What is different ?



1. Gender Differences : Genetic Risk Profiles for CVD

- **Estimate whether the genetic risk profiles of CVD differ between the genders**

False discovery rate analysis between men and women



Primary analysis

: FINRISK 92 & 97 case-cohort sets

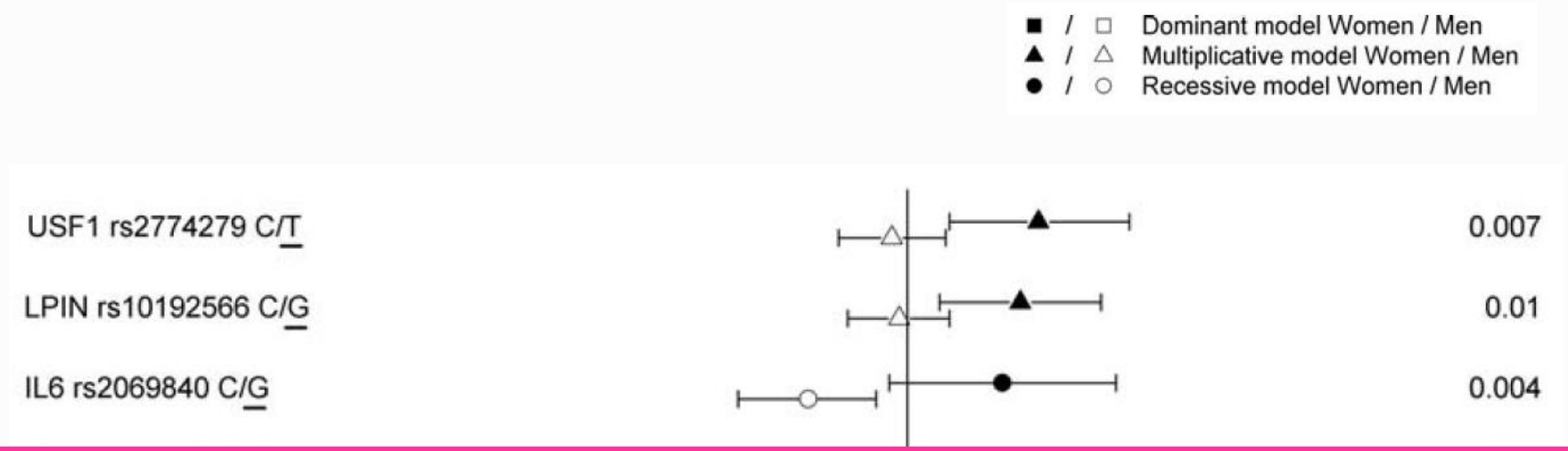
- Time to event analysis for CVD
- **Genotype-sex interaction analysis for CVD**
- Association with quantitative CVD risk factors in the subcohort free of disease at baseline
- **Genotype-sex interaction analysis for quantitative CVD risk factors**

Silander K, et al. PLOS ONE 2008;3:3615

1. Gender Differences : Genetic Risk Profiles for CVD

- Estimate whether the genetic risk profiles of CVD differ between the genders

Gender-specific association between variants and CVD



Genetic risk loci for CVD are more detectable in women, while for men they are more confounded by environmental/lifestyle risk factors.

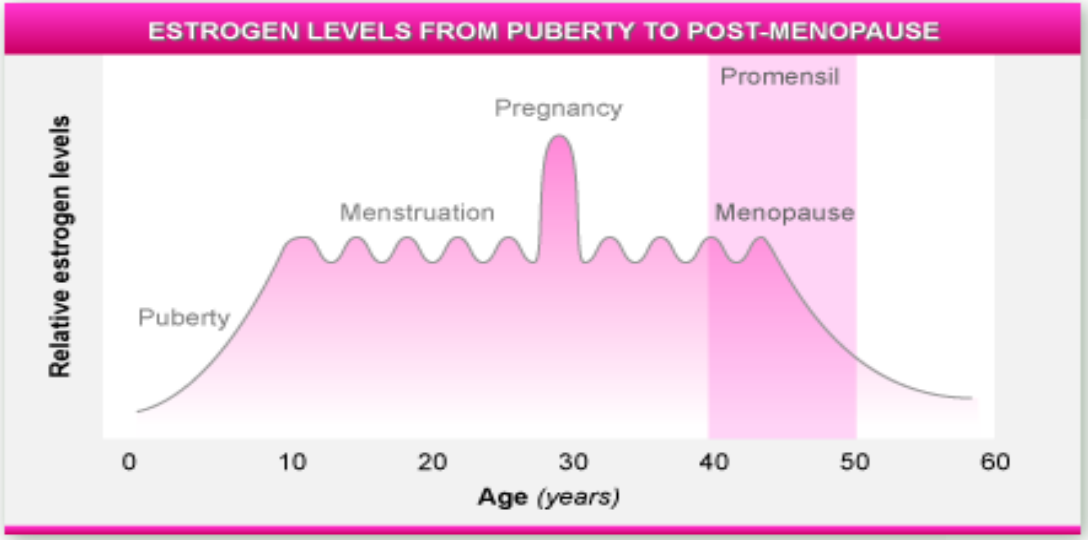
Silander K, et al. PLOS ONE 2008;3:3615

2. Hormonal Differences : Menopause

- Exposure to endogenous estrogens delays the manifestation of atherosclerotic disease in women
- Women with an early menopause (<40 years)

  ➔ 2 year lower life expectancy compared with women with a normal or late menopause
- Young women with endogenous estrogen deficiency 7x increase in coronary artery risk

Gouva L. et al. HORMONES 2004;3:171-183



2. Hormonal Differences : Menopause

- Menopause

Body weight

Central obesity

LDL ↑
HDL→

Body fat distribution change

Upregulation of RAS system

Increased ischemic heart disease

2. Hormonal Differences : Menopause

- **Sexual hormones: Effects on cardiac and mitochondrial activity after ischemia–reperfusion in adult rats. Gender difference**

Influence of sex hormones on heart and mitochondrial functions, from adult castrated female and male, and intact rats

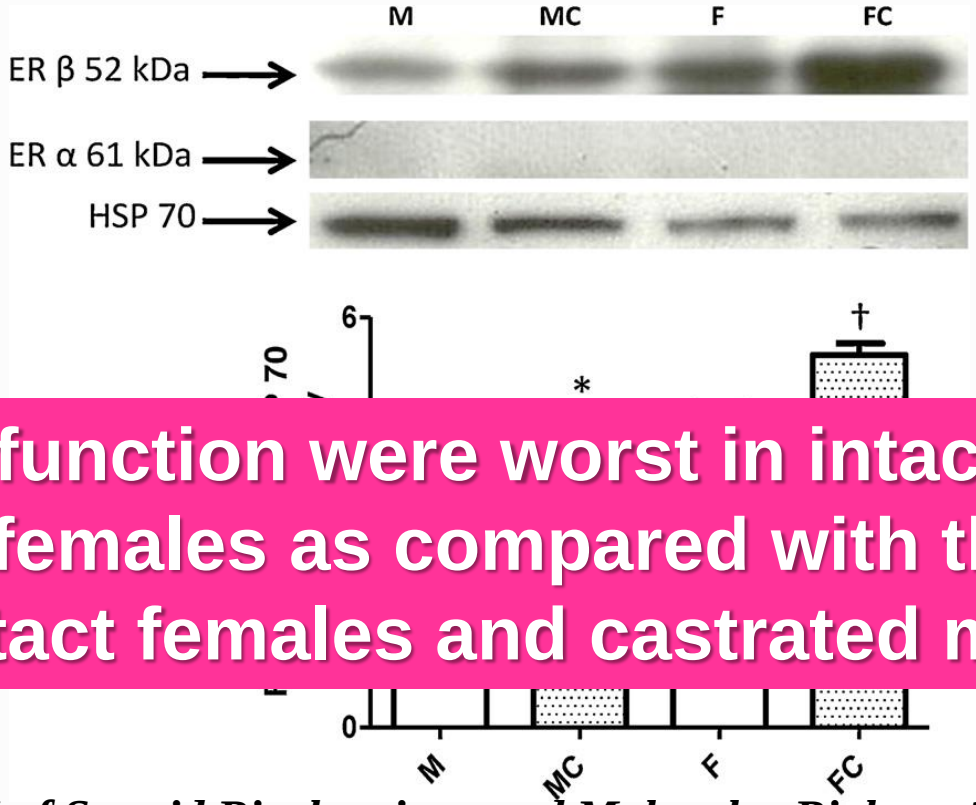
- **Mitochondria are involved in cell survival and are important targets for estrogen actions.**
- **Estrogen receptor has been described in mitochondria of different kinds of cells, such as primary cardiomyocytes.**

Pavon N, et al. J of Steroid Biochemistry and Molecular Biology. 2012;132:135-146

2. Hormonal Differences : Menopause

- **Sexual hormones: Effects on cardiac and mitochondrial activity after ischemia–reperfusion in adult rats. Gender difference**

Western blot analysis of ER α and ER β from intact and castrated, female and male rats mitochondria



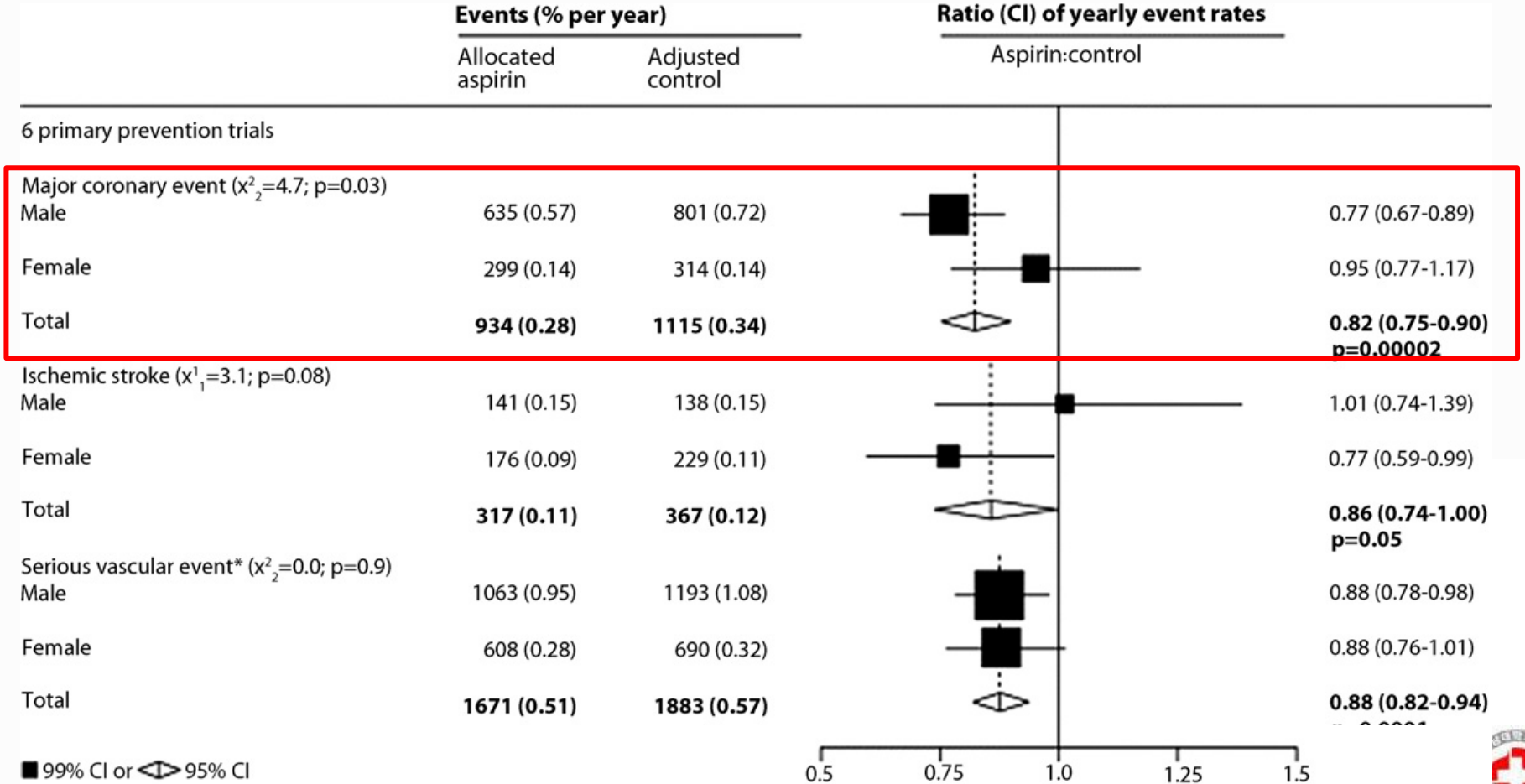
Cardiac function were worst in intact males and castrated females as compared with those found in intact females and castrated males.

Pavon N, et al. J of Steroid Biochemistry and Molecular Biology. 2012;132:135-146

3. Gender differences in anticoagulation and antithrombotic Tx

- Platelet Biology and Response to Antiplatelet Therapy in Women

Selected outcomes in primary prevention trials of aspirin, by sex

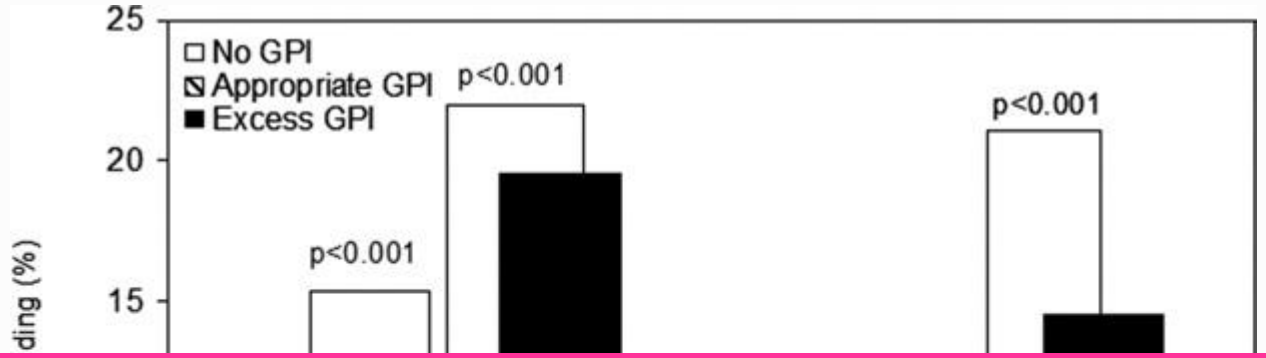


Wang TY, et al. JACC 2012;59:891-900

3. Gender differences in anticoagulation and antithrombotic Tx

- Platelet Biology and Response to Antiplatelet Therapy in Women

Major bleeding by sex and GPI dosing



Women respond differently from men to antithrombotic therapies – showing a greater propensity for bleeding, even c/ appropriate dosing, and differential benefit in terms of prevention of ischemic events.

Wang TY, et al. JACC 2012;59:891-900

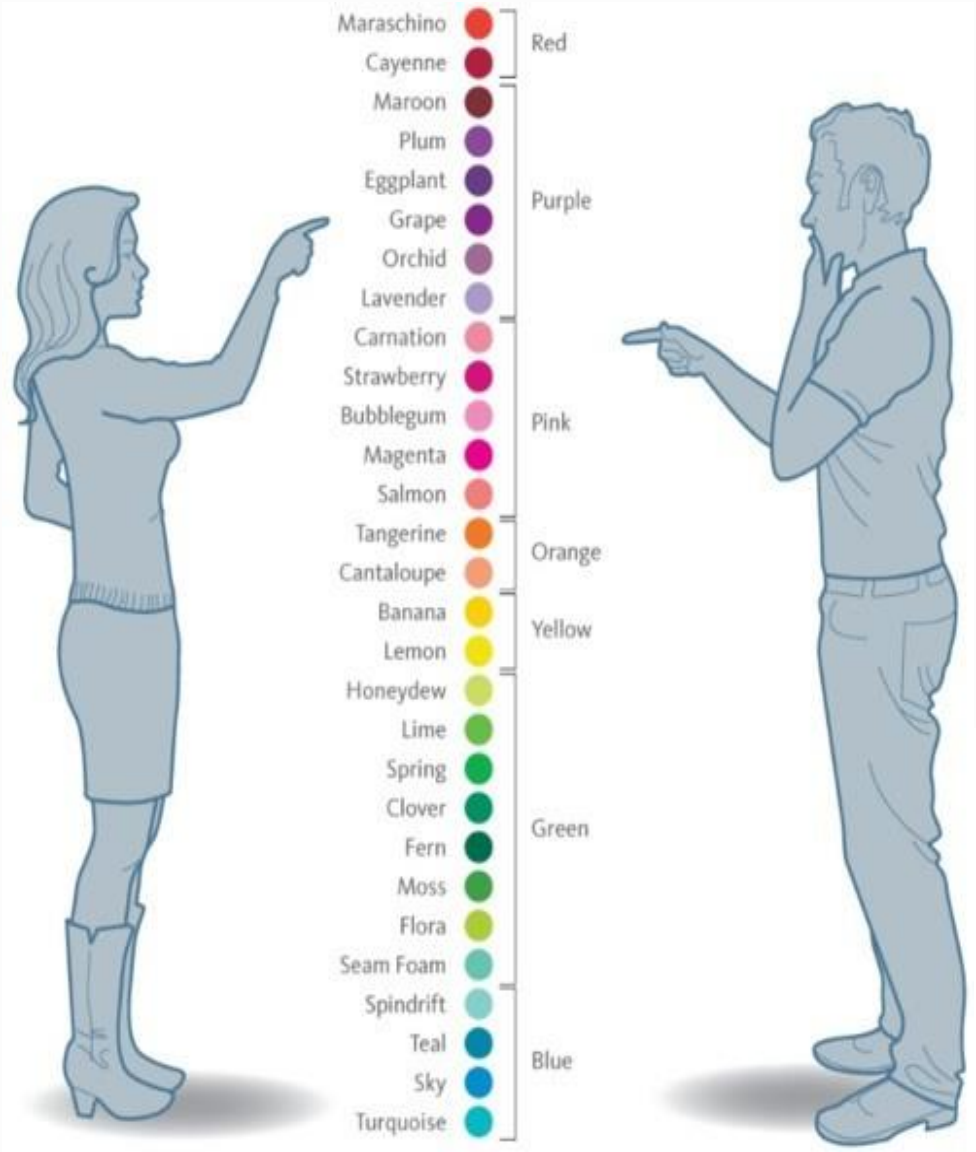
5. Female-specific risk factors

Polycystic ovary disease

Hypertensive disease in pregnancy

Gestational diabetes

여성은 이렇게 많은 색을 구분할 수 있습니다



6. Gender Differences in Symptoms

- Presenting symptoms among patients with documented MI without chest pain

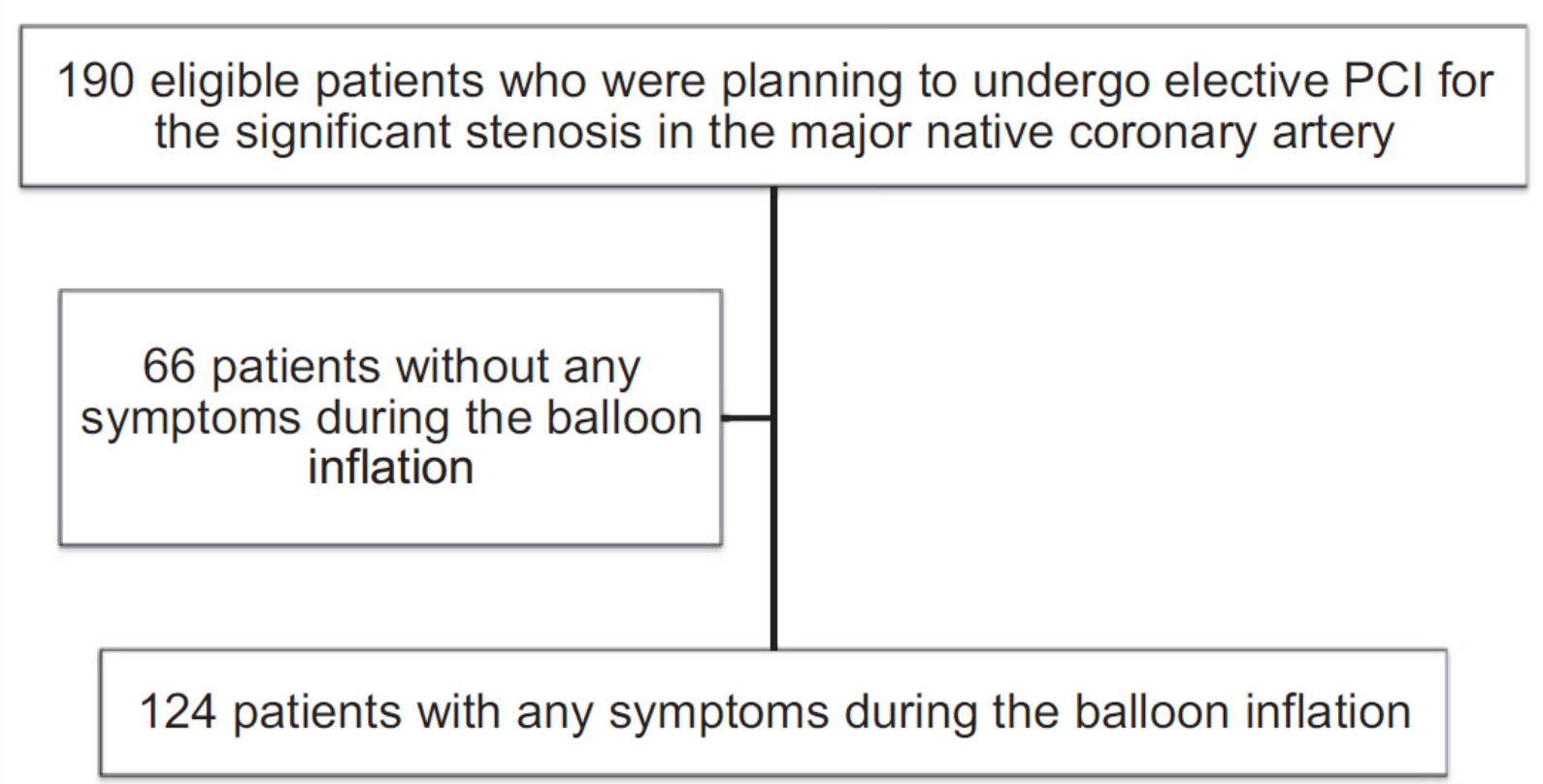
	682 men	344 women	p value
Presyncope	144 (21%)	76 (22%)	0.75
Dyspnea	282 (41%)	144 (42%)	0.89
Palpitation	29 (4.3%)	21 (6.1%)	0.22
Jaw pain	27 (4.0%)	36 (10%)	<0.001
Nausea or vomiting	154 (23%)	111 (32%)	0.001
Diaphoresis	203 (30%)	83 (24%)	0.07

Women with ACS more likely to have atypical symptom
→ Sometimes misdiagnosed, delayed treatment

Heart 2009;95:20–26.

6. Gender Differences in Symptoms

- **Gender Differences in Symptoms During 60-Second Balloon Occlusion of the Coronary Artery**



Tamura A, et al. Am J Cardiol. 2013

6. Gender Differences in Symptoms

Incidence of chest pain and non-chest pain symptoms during 60-second balloon inflation

Variable	Men (n = 72)	Women (n = 52)	p Value
Chest pain	72 (100)	50 (96)	0.96
Non−chest pain symptoms	10 (14)	16 (31)	0.02
Right shoulder/upper arm pain	0 (0)	3 (6)	0.07
Left shoulder/upper arm pain	8 (11)	4 (8)	0.76
Jaw pain	1 (1)	0 (0)	1.00
Neck/throat pain	4 (6)	8 (15)	0.12

Non-chest pain symptoms during the 60-second balloon occlusion of the coronary artery were more common in women than in men, supporting the presence of the gender difference in myocardial ischemic symptoms

Tamura A, et al. Am J Cardiol. 2013

7. Gender Differences in coronary lesion

- Gender and the Extent of Coronary Atherosclerosis, Plaque Composition, and Clinical Outcomes in ACS

Baseline QCA Characteristics of NC Lesions According to Sex

	Univariate Analysis			Female Sex in Multivariable Analysis		
	Men	Women	p Value	Coefficient	SE	p Value
All NC lesions	n = 1,417	n = 397				
Number of NC lesions	2.72 ± 2.03	2.38 ± 1.84	0.05	−0.509	0.183	0.0053
Vessels with NC lesions	1.46 ± 0.98	1.29 ± 0.98	0.048	−0.282	0.091	0.0001
Total length of NC lesions, mm	20.6 [9.0–38.4]	16.6 [7.0–30.6]	0.008	−0.825	1.713	0.0001
Lesion location						
Right coronary artery	28.9% (410/1,417)	27.2% (108/397)	0.50	—	—	—
Left main artery	0.6% (8/1,417)	0.3% (1/397)	0.69	—	—	—
Left anterior descending artery	39.1% (554/1,417)	43.3% (172/397)	0.13	—	—	—
Left circumflex artery	31.4% (445/1,417)	29.2% (116/397)	0.41	—	—	—
Lesion length, mm	8.3 [5.7–12.4]	7.6 [5.1–11.3]	0.01	−1.747	0.690	0.011
Reference vessel diameter, mm	2.3 [1.9–2.8]	2.2 [1.8–2.7]	0.01	−0.005	0.062	0.936
Minimal luminal diameter, mm	1.4 [1.1–1.9]	1.4 [1.0–1.8]	0.08	0.041	0.059	0.491
Diameter stenosis, %	37.4 [31.8–46.3]	37.3 [31.9–46.9]	0.77	—	—	—

Lansky AJ, et al. J Am Coll Cardiol Img 2012;5:S62-72

7. Gender Differences in coronary lesion

Baseline IVUS Characteristics of Coronary Tree According to Sex

	Univariate Analysis			Female Sex in Multivariable Analysis		
	Men (n = 508)	Women (n = 152)	p Value	Coefficient	SD Error	p Value
Total IVUS length analyzed, mm	175.5 [137.4–217.2]	166.5 [125.3–210.4]	0.07			
Number of NC lesions/patient	5 [4–6]	4 [3–6]	0.002	−0.509	0.183	0.005
Echolucent NC plaques	17.5% (89/508)	13.8% (21/152)	0.28	—	—	—
Ruptured NC plaques	16.3% (83/508)	6.6% (10/152)	0.002	−0.949	0.330	0.004
Number of NC lesions	2,558	671				
Lesion length, mm	11.5 [5.9–21.8]	10.6 [5.2–20.5]	0.05	—	—	—
MLA, mm^2	6.0 [4.4–8.3]	5.2 [4.0–7.0]	<0.0001	−0.830	0.145	<0.0001
MLA <4 mm^2	18.6% (475)	24.1% (162)	0.001	0.307	0.125	0.014
MLD, mm	2.5 [2.1–3.0]	2.3 [2.0–2.7]	<0.0001	0.041	0.050	0.401
Remodeling index	0.93 [0.85–1.00]	0.94 [0.85–1.00]	0.65	—	—	—

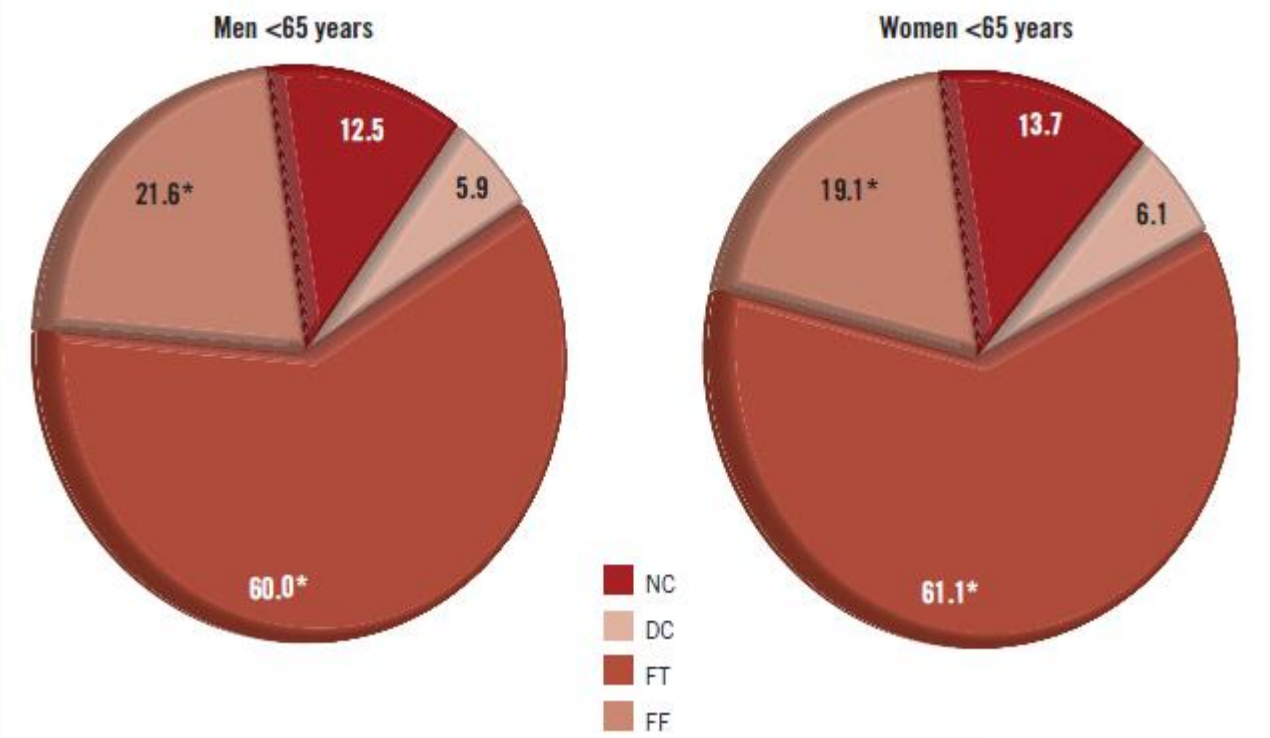
Women have less extensive coronary artery disease by angiographic and IVUS measures, and that lesions in women compared with men have less plaque rupture, less necrotic core and calcium, similar plaque burden, and smaller lumens. TCFA was a stronger marker of plaque vulnerability

Lansky AJ, et al. J Am Coll Cardiol Img 2012;5:S62-72

7. Gender Differences in coronary lesion

- Age- and gender-related changes in plaque composition in patients with acute coronary syndrome: the PROSPECT study

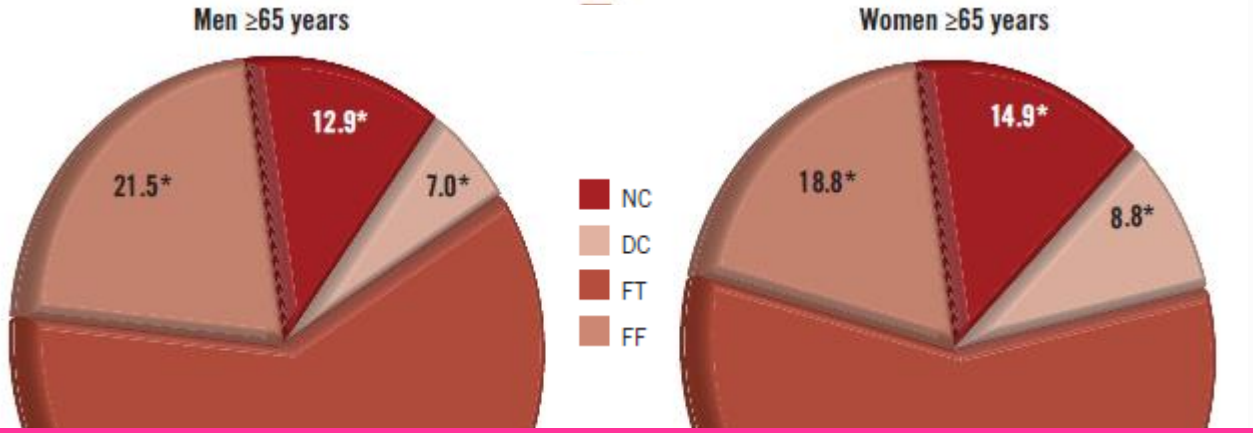
Distribution of the four VH-IVUS plaque components in the non-culprit lesions according to gender



Ruiz-García J, et al. Eurointervention 2012;8:929-938

7. Gender Differences in coronary lesion

Distribution of the four VH-IVUS plaque components in the non-culprit lesions according to gender

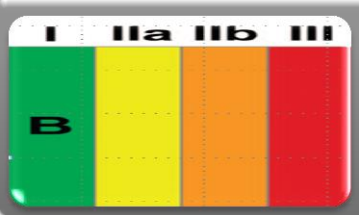


Gender-specific differences in the extent and composition of coronary plaque are present in patients <65 years (but not ≥65 years) of age:
Man had a greater number of fibroatheromas and NCLs per patient with larger plaque volumes, and fewer fibrotic plaques than women in the same age group.

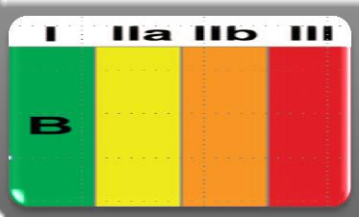
Ruiz-García J, et al. Eurointervention 2012;8:929-938

8. Gender Differences in treatment

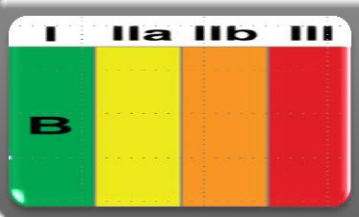
- **2007 ACC/AHA Guideline - UA/NSTEMI (For women)**



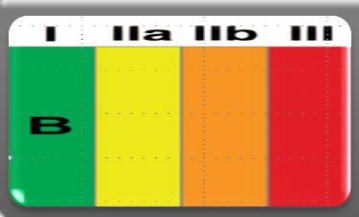
Women with UA/NSTEMI should be managed with the same pharmacological therapy as men both in the hospital and for secondary prevention



Recommended indications for noninvasive testing in women with UA/NSTEMI are similar to those for men



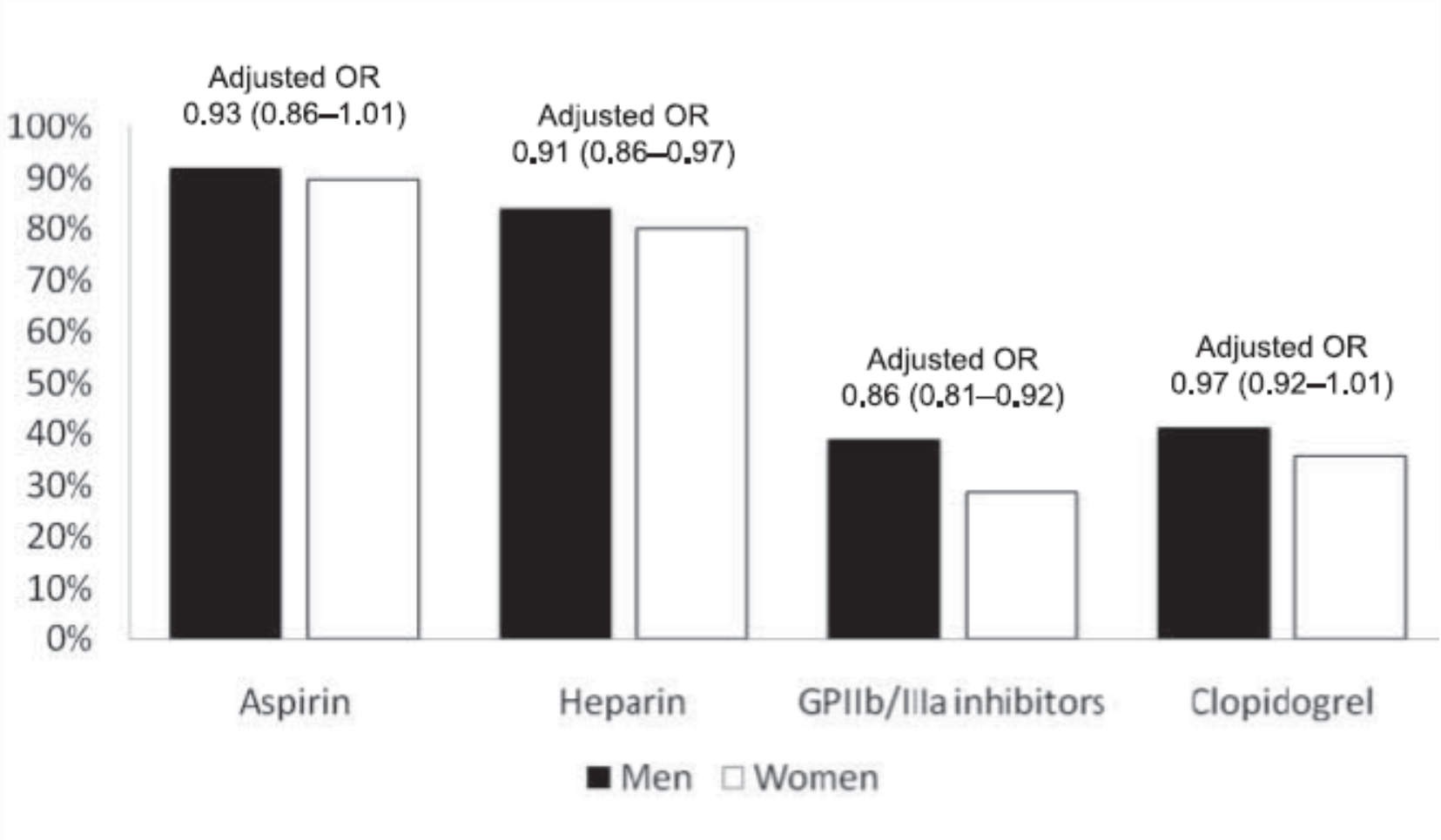
For women with high risk features, recommendations for invasive strategy are similar to those of men



For women with low risk features, a conservative strategy is recommended

8. Gender Differences in treatment

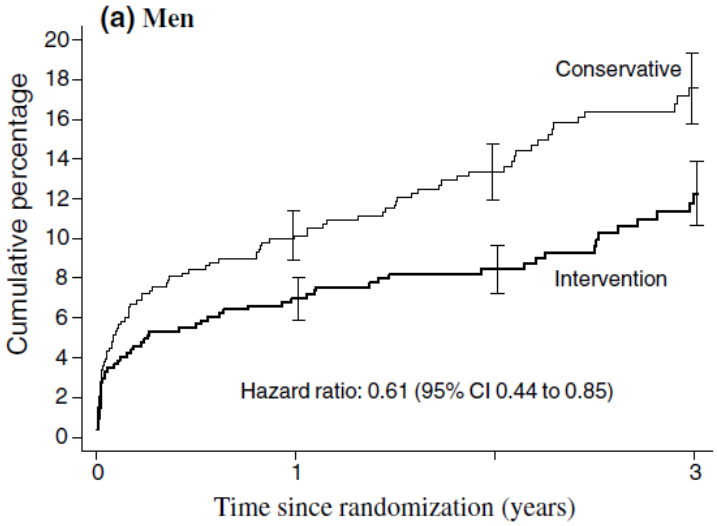
- Use of medical treatment by gender in the CRUSADE study

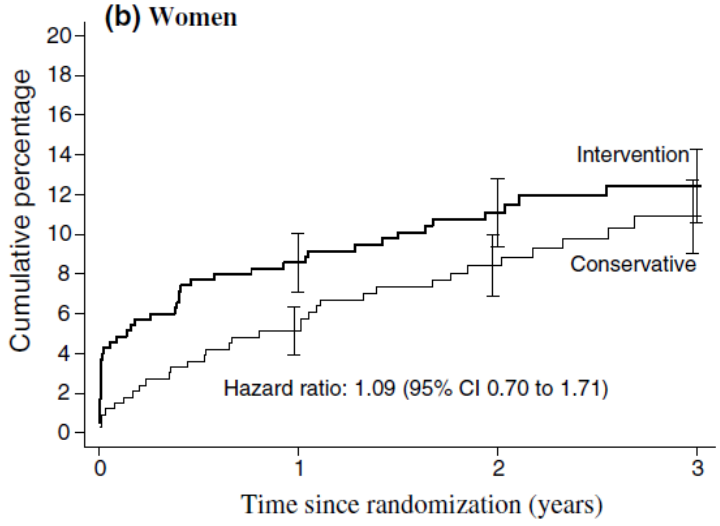


Capodanno D et al. Thromb Haemost 2010;104:471-484

8. Gender Differences in treatment

- Do men benefit more than women from an interventional strategy in patients with UA or NSTEMI?





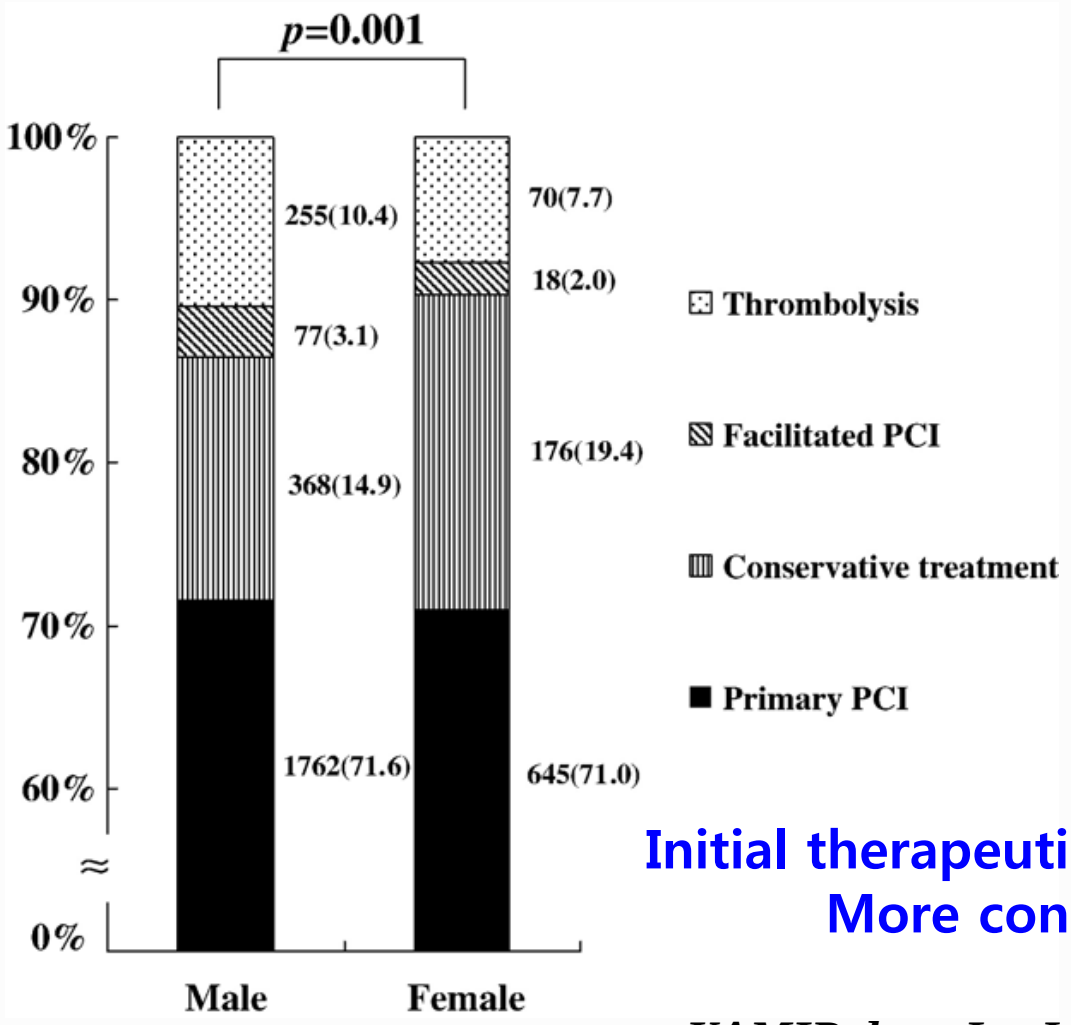
Intervention	545	491	354	189	350	316	228	125	

An early intervention strategy resulted in a beneficial effect in men which was not seen in women although caution is needed in interpretation.

Eur Heart J. 2004;25:1641–50

8. Gender Differences in treatment

- Gender differences of success rate of PCI and short term cardiac events

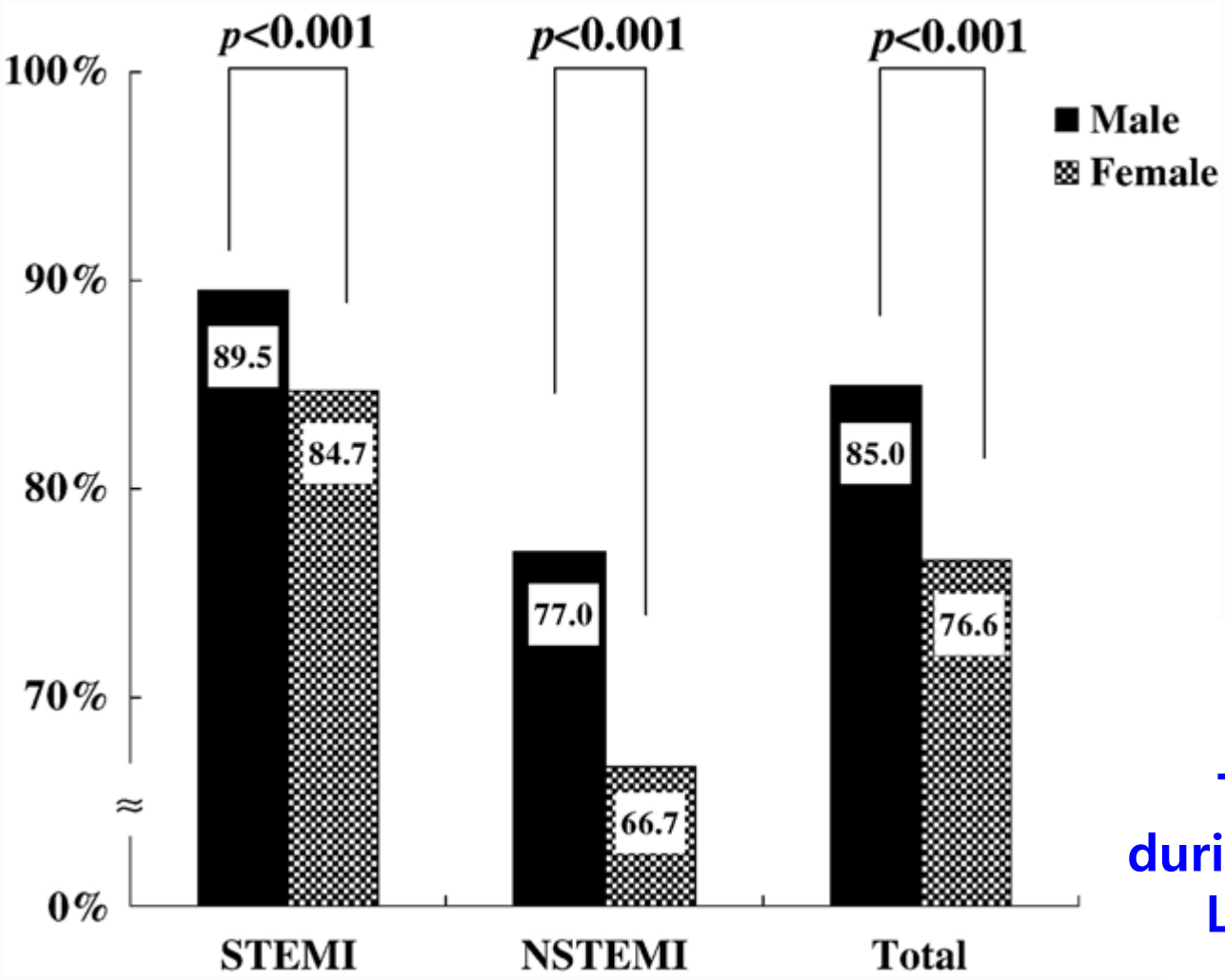


Initial therapeutic strategy in acute STEMI: More conservative in female

KAMIR data. Int J Cardiol. 2008;130:227-234

8. Gender Differences in treatment

- Gender differences of success rate of PCI and short term cardiac events



The rate of PCI during hospitalization: Lower in female

KAMIR data. Int J Cardiol. 2008;130:227-234

8. Gender Differences in treatment

- One month clinical follow-up for the development of MACEs

	STEMI			NSTEMI		
	Male (n=2493)	Female (n=918)	p value	Male (n=1405)	Female (n=765)	p value
Cardiac death	139 (5.6%)	116 (12.6%)	<0.001	49 (3.5%)	54 (7.1%)	<0.001
MI	19 (0.8%)	6 (0.7%)	0.742	15 (1.1%)	15 (2.0%)	0.089
Re-PCI	27 (1.1%)	8 (0.9%)	0.587	10 (0.7%)	6 (0.8%)	0.850
CABG	2 (0.1%)	0 (0.0%)	0.391	7 (0.5%)	1 (0.1%)	0.177
Total MACE	229 (9.2%)	156 (17.0%)	<0.001	102 (7.3%)	92 (12.0%)	<0.001

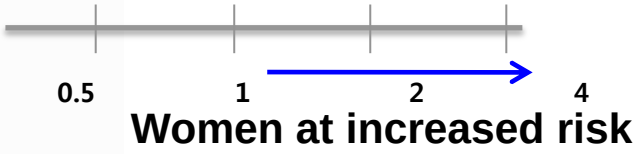
One month MACE was higher in females than males in Korea.

KAMIR data. Int J Cardiol. 2008;130:227-234

Is There (real) Gender Difference in Prognosis of IHD?

Sex Differences in Management and Mortality of Patients With ST-Elevation Myocardial Infarction (from the Korean Acute Myocardial Infarction National Registry)

Adjustment Model	Haxard Rations(95% CI)	p	c-stat
Unadjusted	2.08(1.86-2.34)	<0.001	0.58
Adjustment Model 1' : age only	1.28(1.13-1.44)	<0.001	0.70
Adjustment Model 2'' : age and medical history	1.09(0.96-1.24)	0.376	0.77
Adjustment Model 3† : age, medical history, and hemodynamic	1.02(0.90-1.16)	0.76	0.81
Adjustment Model 4‡ : age, medical history, hemodynamic and clinical performance	1.02(0.89-1.17)	0.798	0.82
Propensity Score-Matched Model	1.00(0.84-1.19)	0.984	



KAMIR/KorMI data. Am J Cardiol. 2012;109:787–793

Is There (real) Gender Difference in Prognosis of IHD?

Clinical Investigations

Gender Differences in Clinical Features and In-hospital Outcomes in ST-segment Elevation Acute Myocardial Infarction: From the Korean Acute Myocardial Infarction Registry (KAMIR) Study

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Department of Internal Medicine, Yeungnam University Hospital, Daegu, Korea (Park, Kim, Shin); Department of Internal Medicine, Chonnam National University Hospital, Kwangju, Korea (Jeong, Ahn); Department of Internal Medicine, Catholic University Hospital, Seoul, Korea (Chung, Seung); Department of Internal Medicine, Kyunghee University Hospital, Seoul, Korea (Kim); Division of Cardiology, Department of Internal Medicine, Chungbuk National University Hospital, Cheongju, Korea (Cho); Department of Internal Medicine, Yonsei University Severance Hospital, Seoul, Korea (Jang, Choi); Department of Internal Medicine, Asan Medical Center, Ulsan University, Seoul, Korea (Park); Department of Internal Medicine, Chungnam National University Hospital, Daejeon, Korea (Seong); Department of Internal Medicine, Kyungpook National University Hospital, Daegu, Korea (Chae); Department of Internal Medicine, Keimyung University Hospital, Daegu, Korea (Hur); Department of Internal Medicine, Busan National University Hospital, Busan, Korea (Hong)

ABSTRACT

Background: Studies have suggested that women are biologically different and that female gender itself is independently associated with poor clinical outcome after an acute myocardial infarction (AMI).

Hypothesis: We analyzed data from the Korean Acute Myocardial Infarction Registry (KAMIR) to assess gender differences in in-hospital outcomes post ST-segment elevation myocardial infarction (STEMI).

Methods: Between November 2005 and July 2007, 4037 patients who were admitted with STEMI to 41 facilities were registered into the KAMIR database; patients admitted within 72 hours of symptom onset were selected and included in this study.

Results: The proportion of patients who had reperfusion therapy within 12 hours from chest pain onset was lower in women. Women had higher rates of in-hospital mortality (8.6% vs 3.2%, $P < .01$), noncardiac death (1.5% vs 0.4%, $P < .01$), cardiac death (7.1% vs 2.8%, $P < .01$), and stroke (1.2% vs 0.5%, $P < .05$) than men. Multivariate logistic regression analysis identified age, previous angina, hypertension, a Killip class $\geq$ II, a left ventricular ejection fraction (LVEF) <40%, and a thrombolysis in myocardial infarction flow (TIMI) grade $\leq$3 after angioplasty as independent risk factors for in-hospital death for all patients; however, female gender itself was not an independent risk factor.

Conclusions: The results of this study show that although women have a higher in-hospital mortality than men, female gender itself is not an independent risk factor for in-hospital mortality.

Although women have a higher in-hospital mortality than men,

female gender itself is not an independent risk factor for in-hospital mortality

KAMIR data. Clin Cardiol. 2010;33: E1–E6

Conclusion

- There seems to be gender difference in IHD between men and women.
- Differences in prognosis between women and men with IHD are currently under attention.
- Still little is known about the prognostic implications of differences.
- Gender-based interpretation is needed to improve therapeutic efficacy and outcomes in women.

Age, years

경청해 주셔서 감사합니다.

Chonnam Nat. Univ. Hosp.

11th Gwangju Interventional Cardiology Symposium (Live demonstration)

Date: 7th - 8th June, 2013

Venue: Myung-Hak Hall, Chonnam National University Medical School, Gwangju