Ipertensione arteriosa e danno d'organo cardiovascolare nella donna

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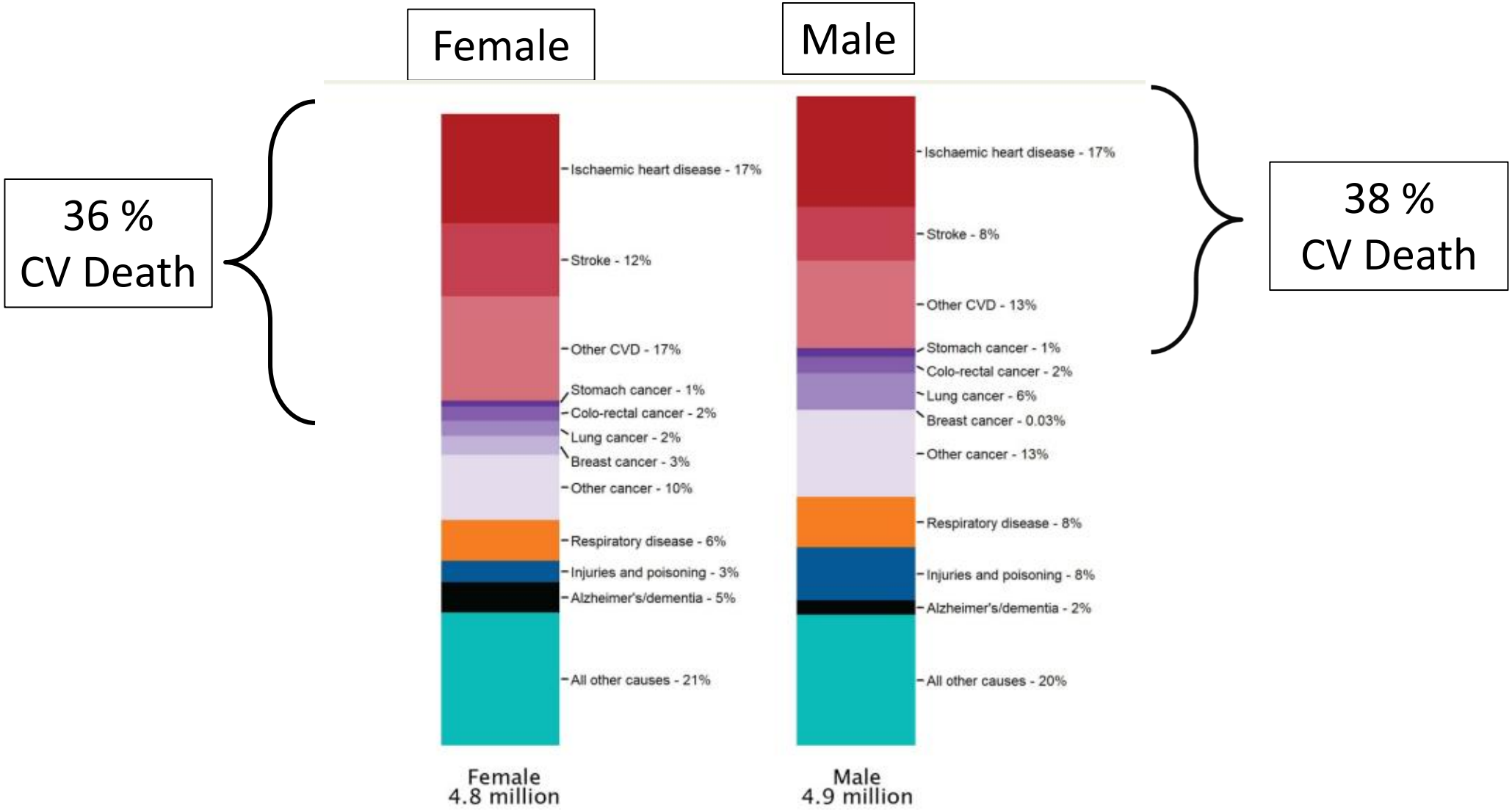
European Society of Cardiology: cardiovascular disease statistics 2021

Timmis ate al European Heart Journal (2022) 43, 716–799

Deaths by cause for all ages in ESC member countries (latest year available)

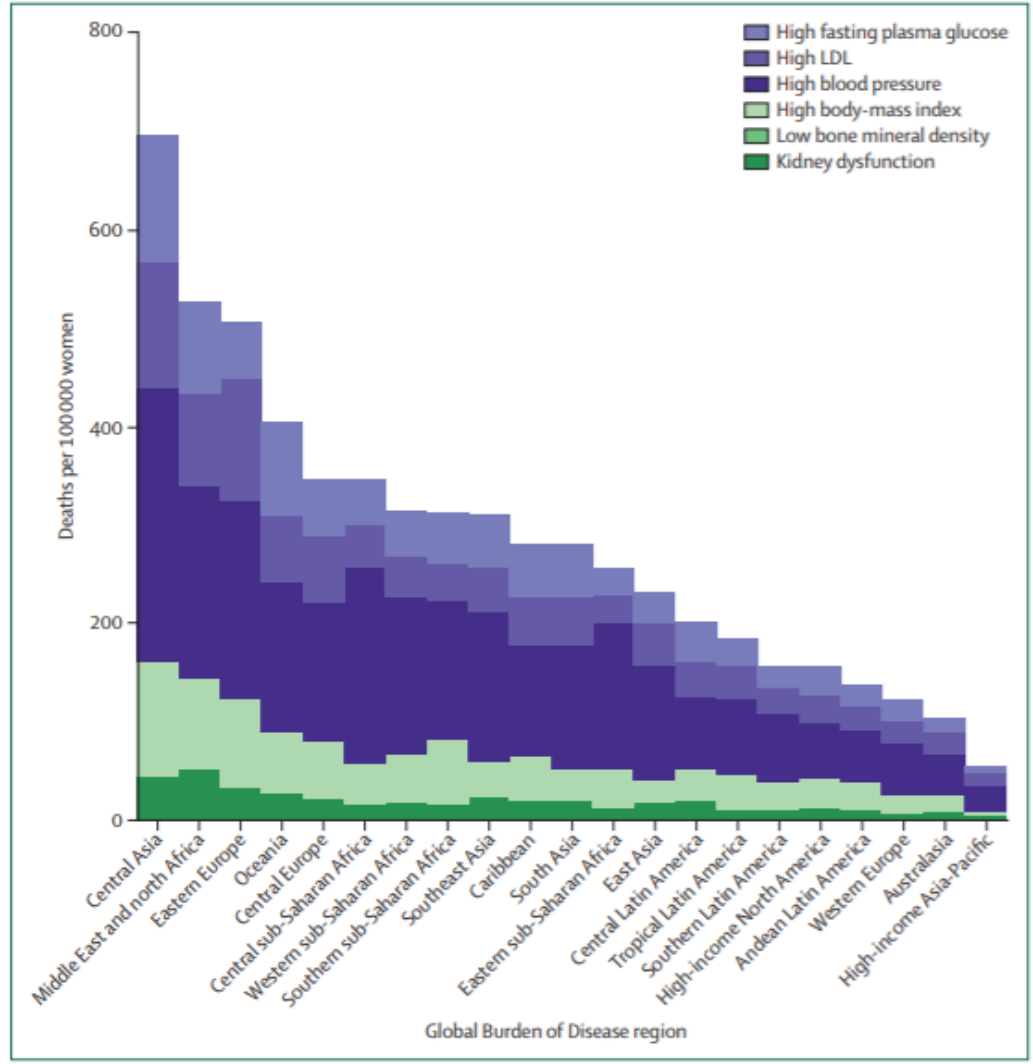
Data source:WHO Mortality Database, https://www.who.int/healthinfo/statistics/mortality_rawdata/en



The *Lancet* women and cardiovascular disease Commission: reducing the global burden by 2030

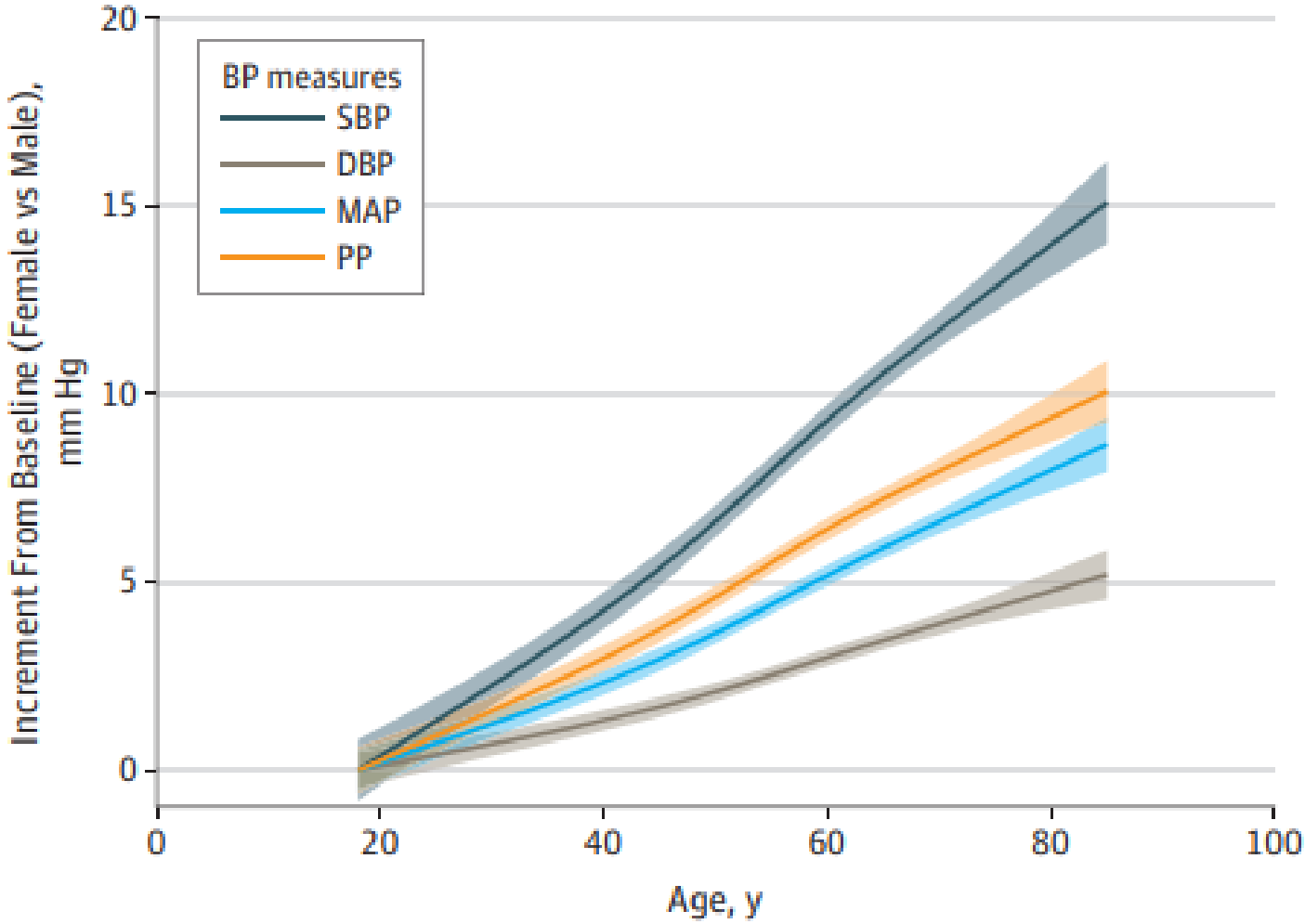
Birgit Vogel, Monica Acevedo, Yolande Appelman, C Noel Bairey Merz, Alaide Chieffo, Gemma A Figtree, Mayra Guerrero, Vijay Kunadian, Carolyn S P Lam, Angela H E M Maas, Anastasia S Mihailidou, Agnieszka Olszanecka, Jeanne E Poole, Clara Saldarriaga, Jacqueline Saw, Liesl Zühlke, Roxana Mehran

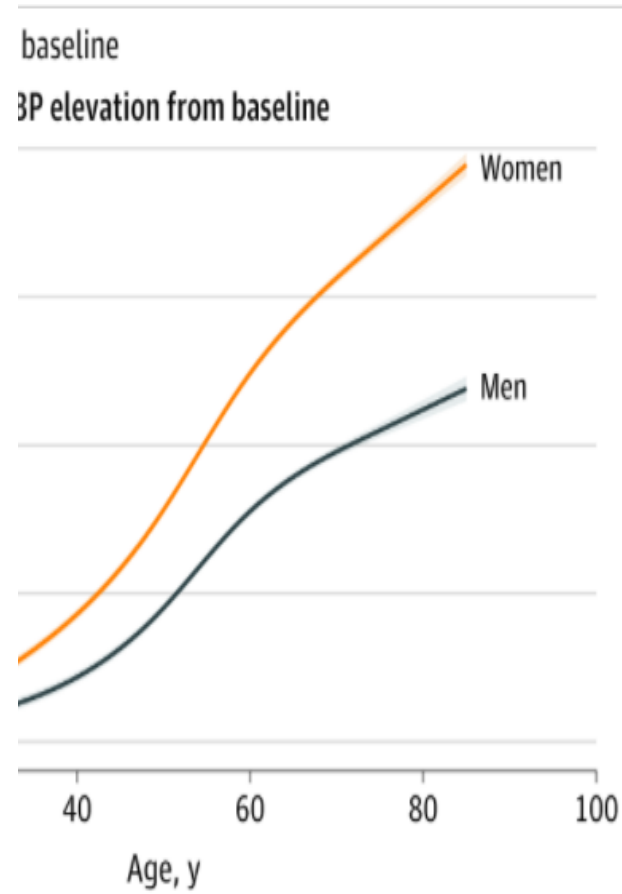
- ***Hypertension is the leading global risk factor for cardiovascular disease morbidity and mortality and is therefore the most substantial and neglected health burden in women.***



Sex Differences in Blood Pressure Trajectories Over the Life Course

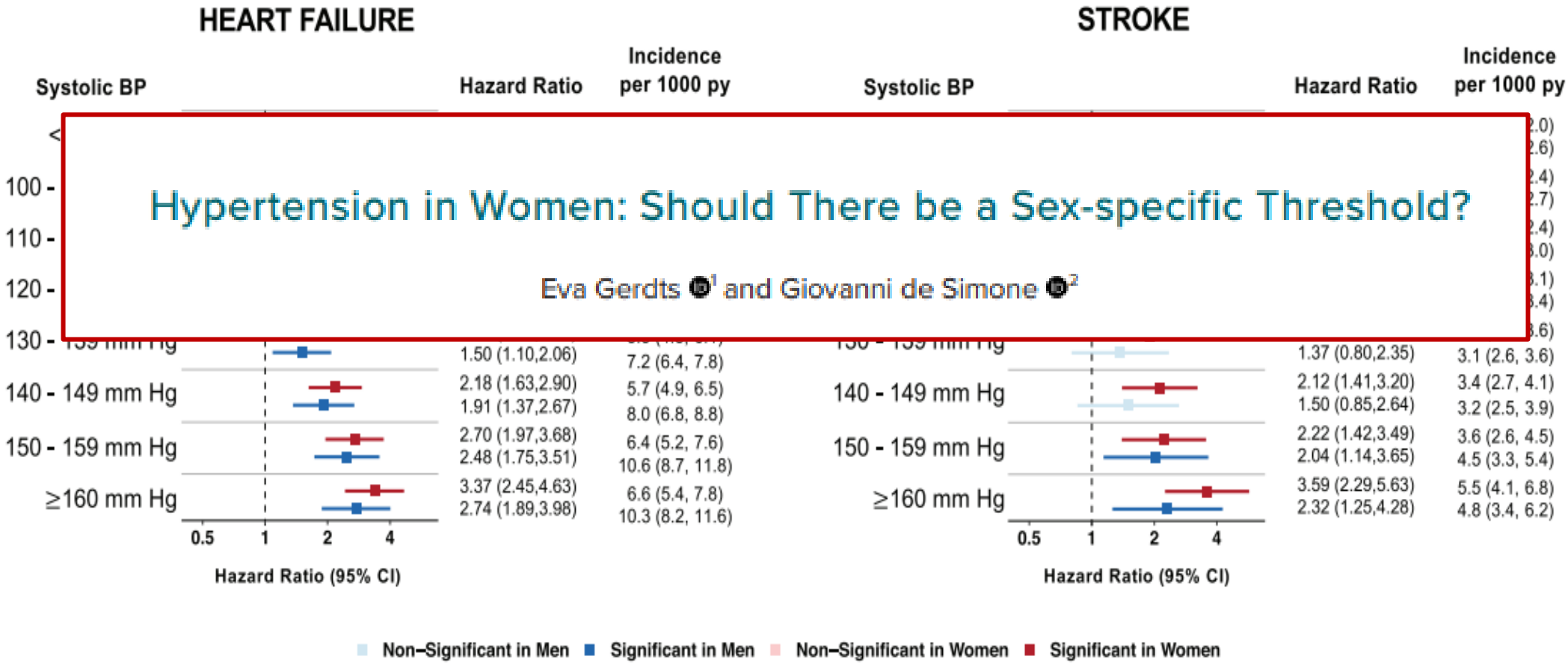
Ji et al, JAMA 2020





Conclusion: "*In contrast with the notion that important vascular disease processes in women lag behind men by 10 to 20 years, sex-specific analyses indicate that BP measures actually progress more rapidly in women than in men, beginning early in life*".

Sex related difference of BP as a risk factor

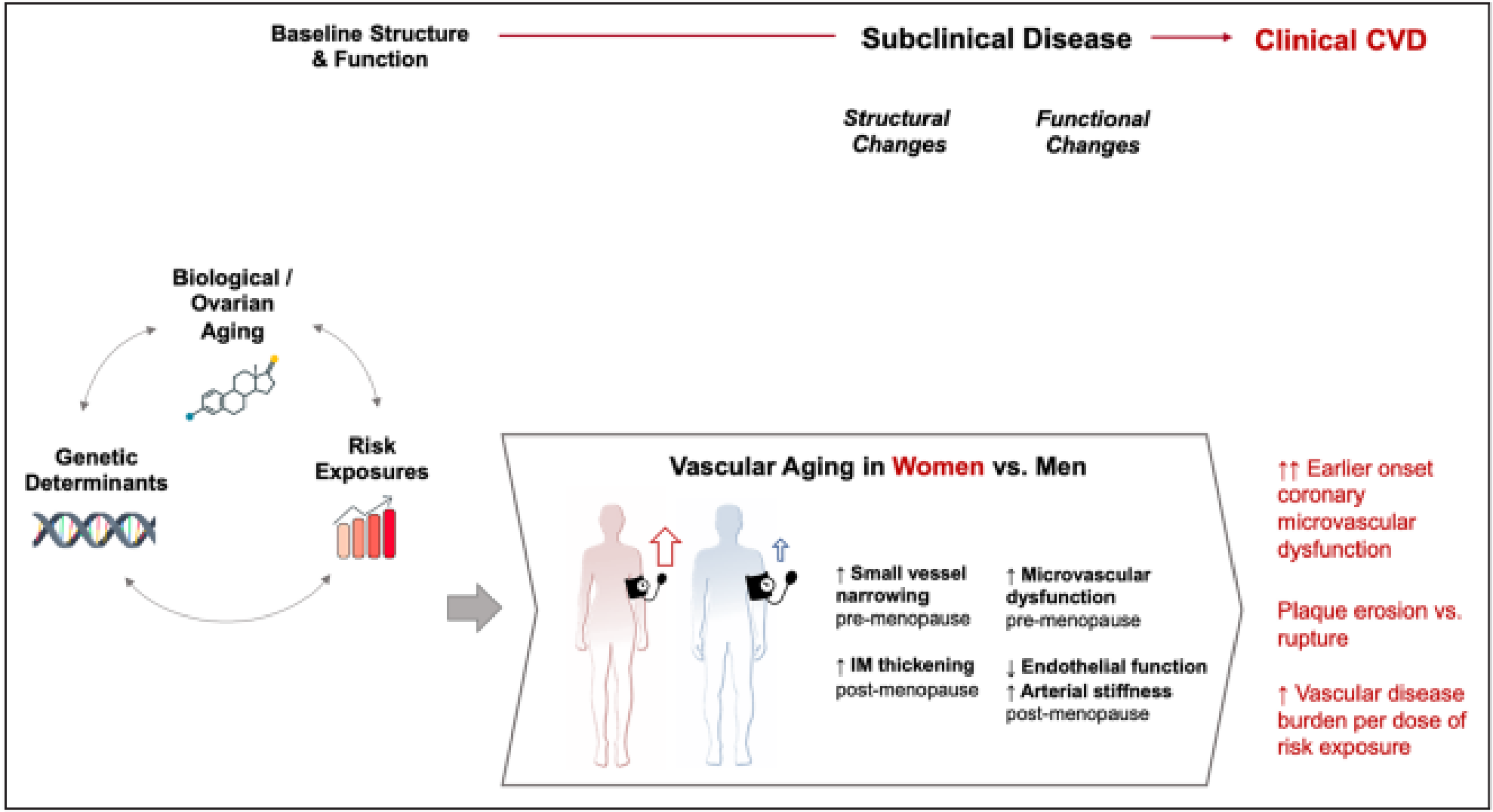


Hypertension in Women: Should There be a Sex-specific Threshold?

Eva Gerdts [1] and Giovanni de Simone [2]

Ji et al Circulation 2021; 143 :761

Cardiovascular aging phenotypes

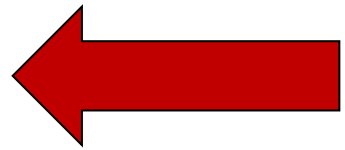


Effectiveness-Based Guidelines for the Prevention of Cardiovascular Disease in Women—2011 Update

A Guideline From the American Heart Association

Risk Status	Criteria
High risk (≥1 high-risk states)	Clinically manifest CHD
	Clinically manifest cerebrovascular disease
	Clinically manifest peripheral arterial disease
	Abdominal aortic aneurysm
	End-stage or chronic kidney disease
	Diabetes mellitus
	10-y Predicted CVD risk ≥10%
At risk (≥1 major risk factor[s])	Physical inactivity
	Family history of premature CVD occurring in first-degree relatives in men <55 y of age or in women <65 y of age
	Metabolic syndrome
	Evidence of advanced subclinical atherosclerosis (eg, coronary calcification, carotid plaque, or thickened IMT)
	Poor exercise capacity on treadmill test and/or abnormal heart rate recovery after stopping exercise
	Systemic autoimmune collagen-vascular disease (eg, lupus or rheumatoid arthritis)
	History of preeclampsia, gestational diabetes, or pregnancy-induced hypertension

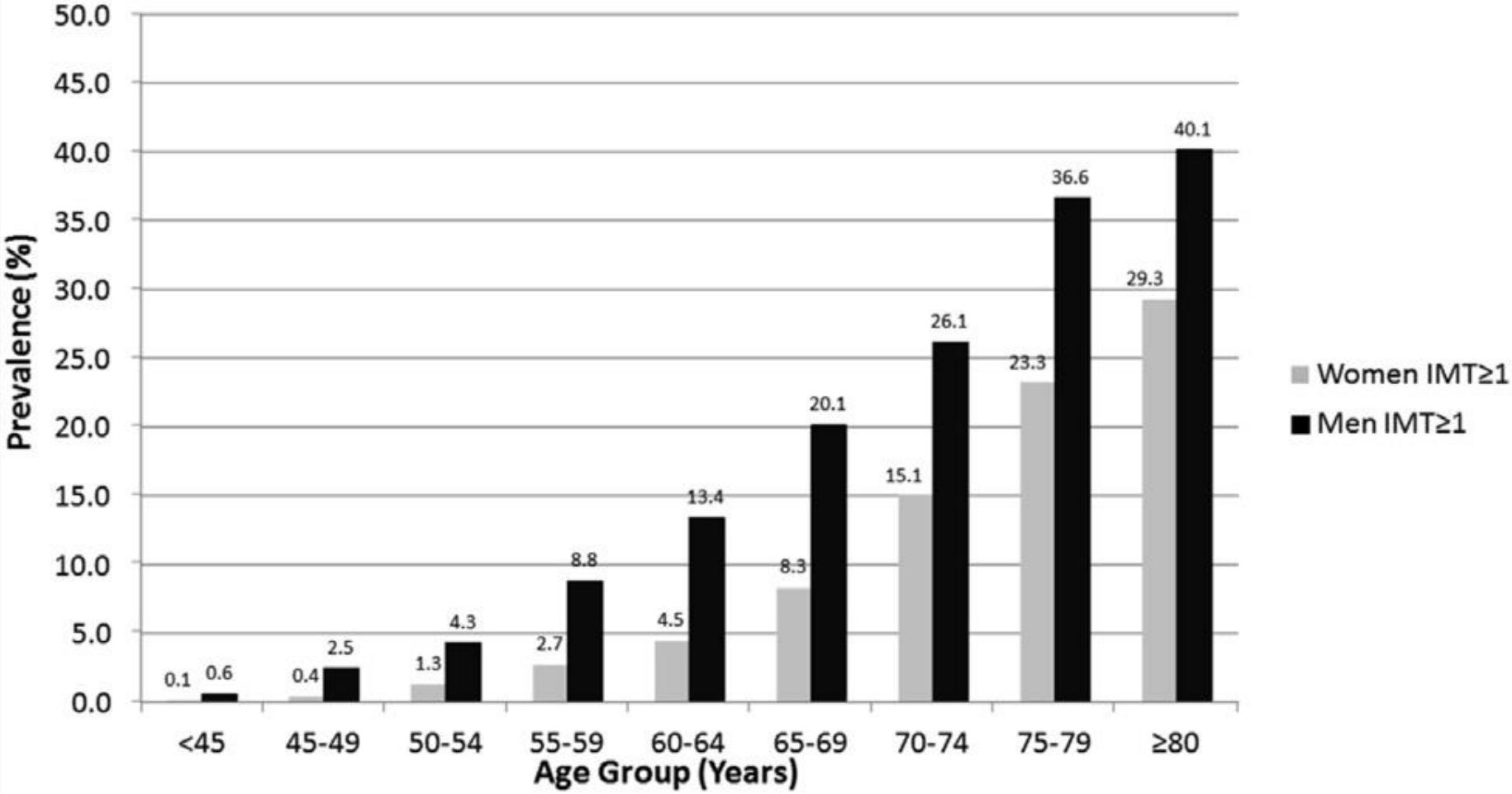
Evidence of advanced subclinical atherosclerosis (eg, coronary calcification, carotid plaque, or thickened IMT)



Mosca et al JACC 2011

Carotid Plaque Characterization, Stenosis, and Intima-Media Thickness According to Age and Gender

9,347 women and 12,676 men



Boulos N et al Am J Cardiol 2016;117:1185e1191

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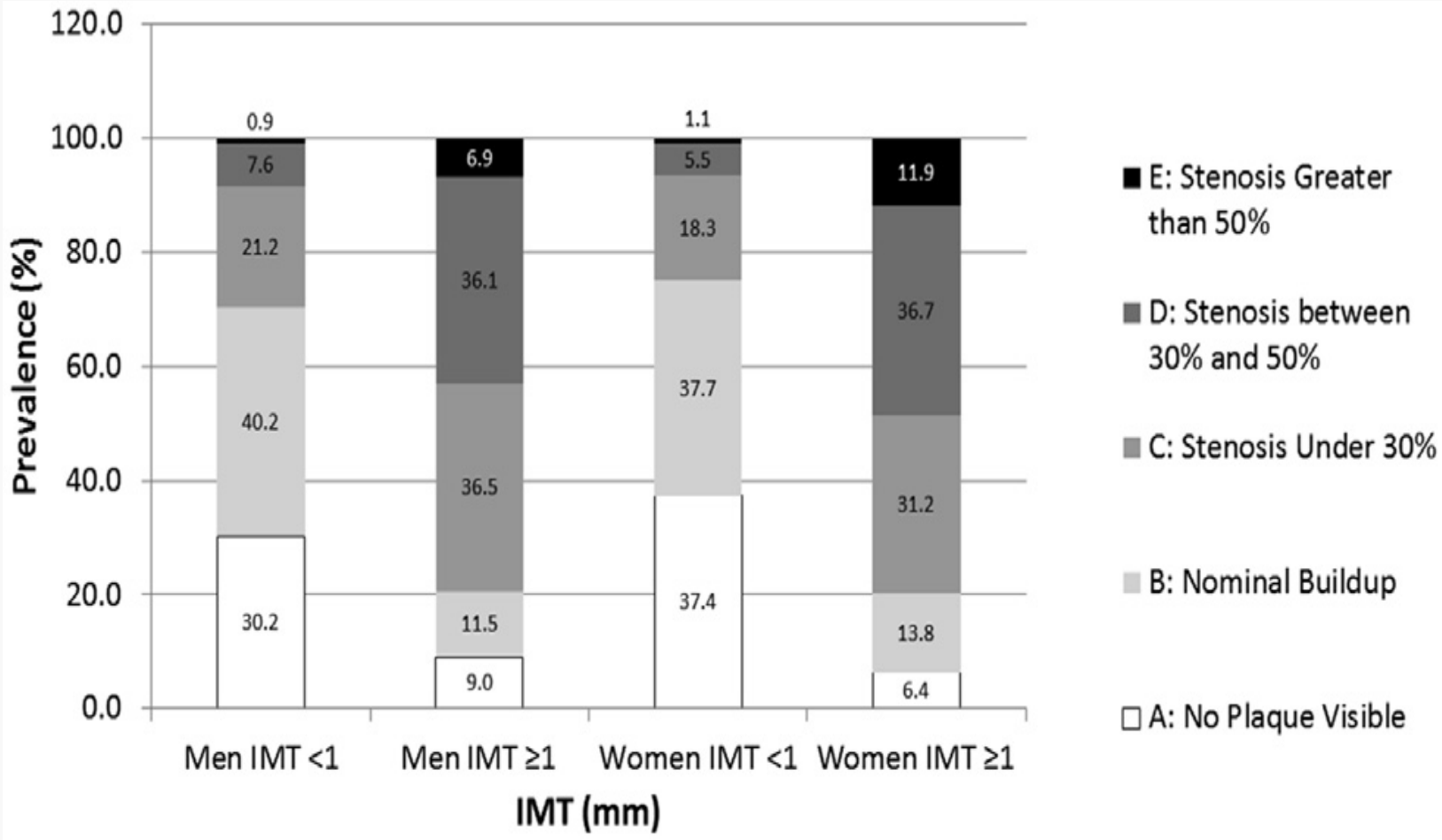
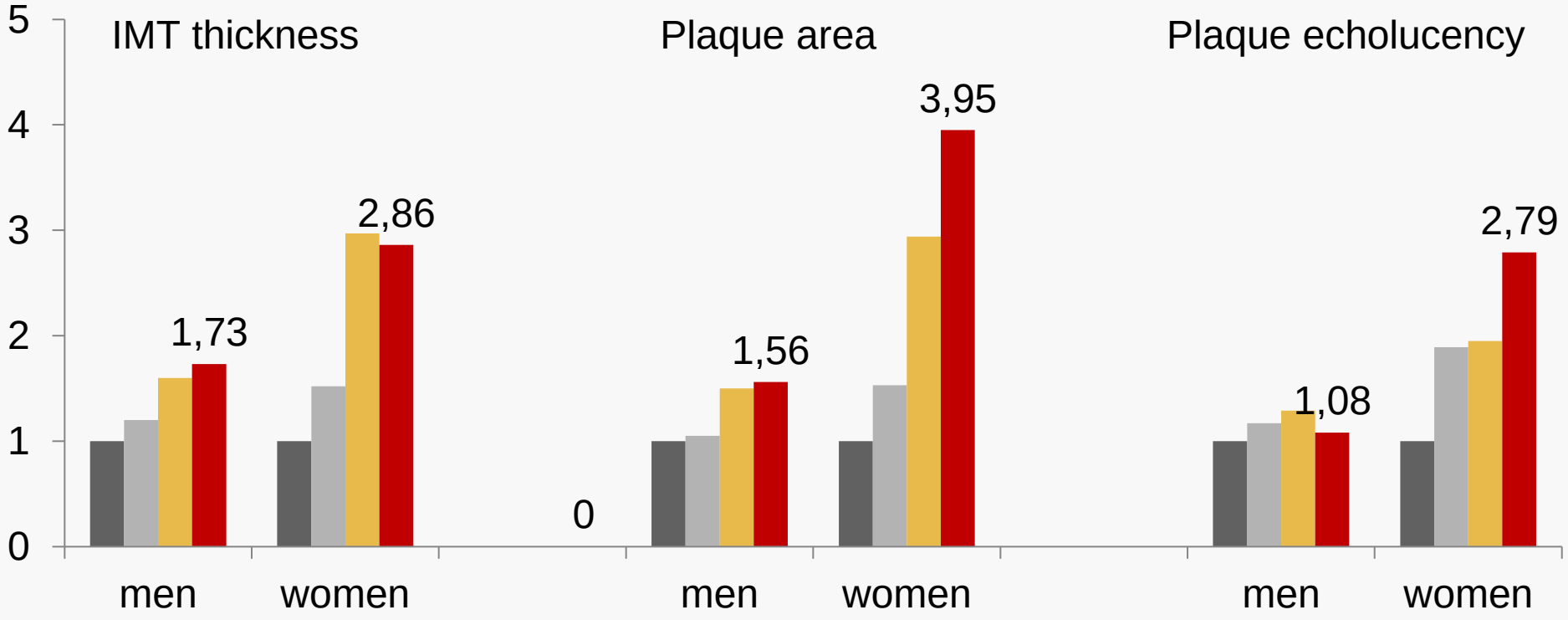


Boulos N et al Am J Cardiol 2016;117:1185e1191

Carotid Atherosclerosis Is a Stronger Predictor of Myocardial Infarction in Women Than in Men
A 6-Year Follow-Up Study of 6226 Persons: The Tromsø Study

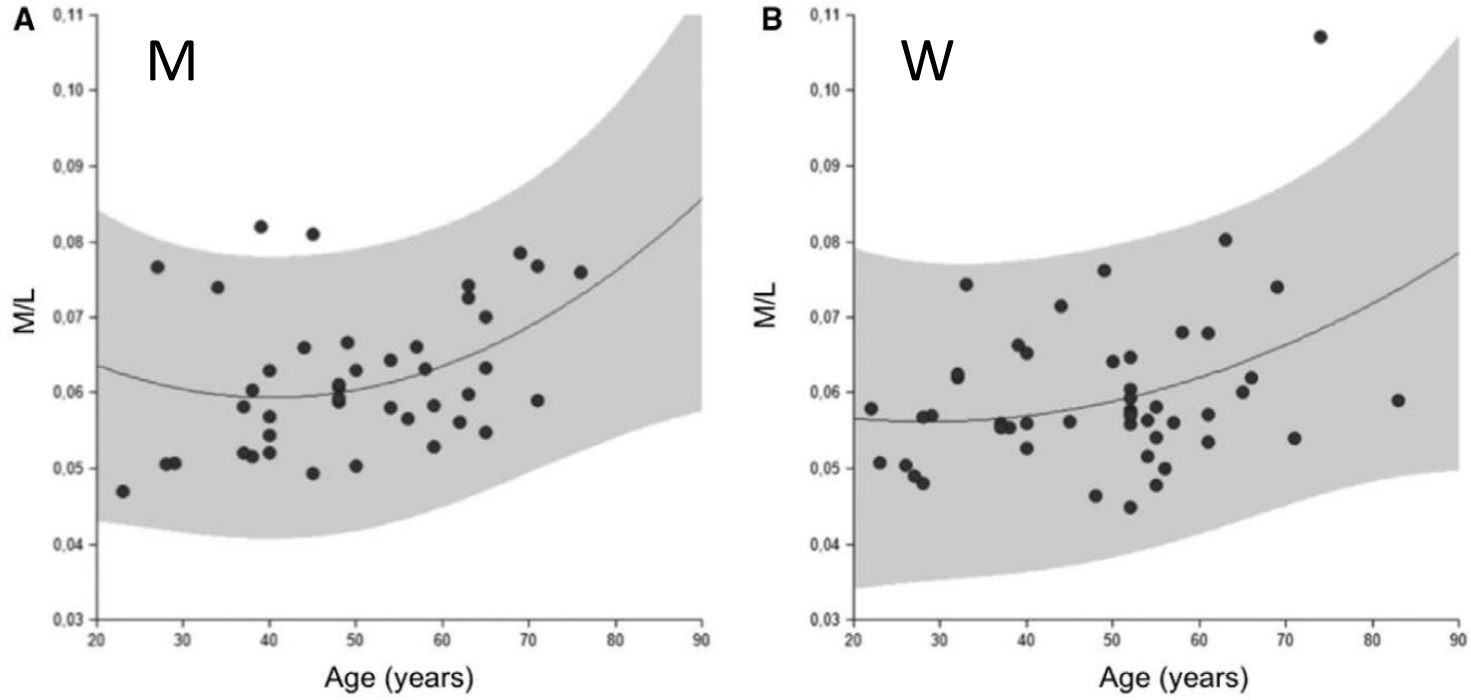
IMT, total plaque area, and plaque echogenicity were measured in 2971 men and 3208 women, aged 25 - 84 years with no previous MI



Stroke. 2007;38:2873-2880

Relationship between Media/Lumen Ratio in Small Arteries and CV Risk Factors

Media/lumen in small arteries obtained in humans by biopsy
91 healthy individuals and 200 individuals with CVRF from 4 Italian SIIA centers



CV risk factors (hypertension, body mass index, total cholesterol, current smoking, fasting blood glucose, SBP) along with **female sex** independently influenced M/L ratio

Bruno RM, et al. Hypertension. 2018;71:1193-1200

Relationship between Media/Lumen Ratio in Small Arteries and CV Risk Factors

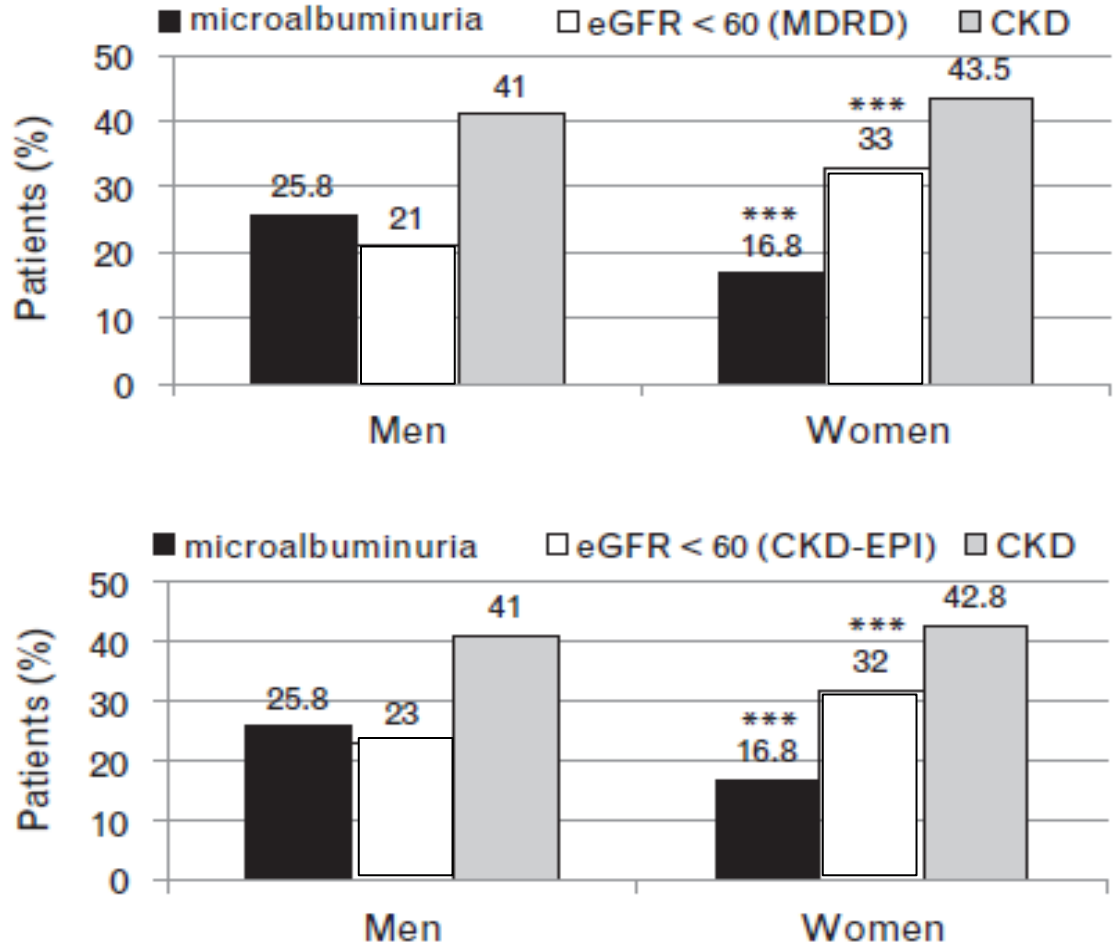
Media/lumen in small arteries obtained in humans by biopsy
91 healthy individuals and 200 individuals with CVRF from 4 Italian SIIA centers

Variable	β Coefficient	Lower 95% CL	Upper 95% CL	r^2	*P* Value
Men					
Heart rate	0.0118	–0.036	0.0595	0.002	0.626
Diastolic BP	0.0097	–0.0458	0.0652	0.001	0.730
Systolic BP	0.0068	–0.0356	0.0493	0.001	0.750
Blood glucose	0.0078	–0.0047	0.0204	0.011	0.218
Triglycerides	0.0008	–0.0083	0.01	0.000	0.856
Total cholesterol	0.0166	0.003	0.0302	0.044	0.017
Smoking	1.3874	0.3793	2.3956	0.055	0.008
BMI	0.1112	0.0475	0.1749	0.089	<0.001
Women					
Heart rate	–0.0185	–0.0653	0.0284	0.005	0.435
Diastolic BP	–0.0652	–0.1326	0.0022	0.031	0.058
Systolic BP	0.0583	0.0208	0.0958	0.079	0.003
Blood glucose	0.0237	0.0102	0.0373	0.101	<0.001
Triglycerides	0.0003	–0.01	0.0107	0.079	0.948
Total cholesterol	–0.0146	–0.0295	0.0003	0.032	0.054
Smoking	0.7507	–0.3722	1.8735	0.015	0.187
BMI	0.0465	–0.0149	0.1079	0.019	0.136

in men, independent determinants of age- and sex-specific M/L Z scores were BMI, T-cholesterol, and smoking, in women, blood glucose and systolic BP play a major role

Bruno RM, et al. Hypertension. 2018;71:1193-1200

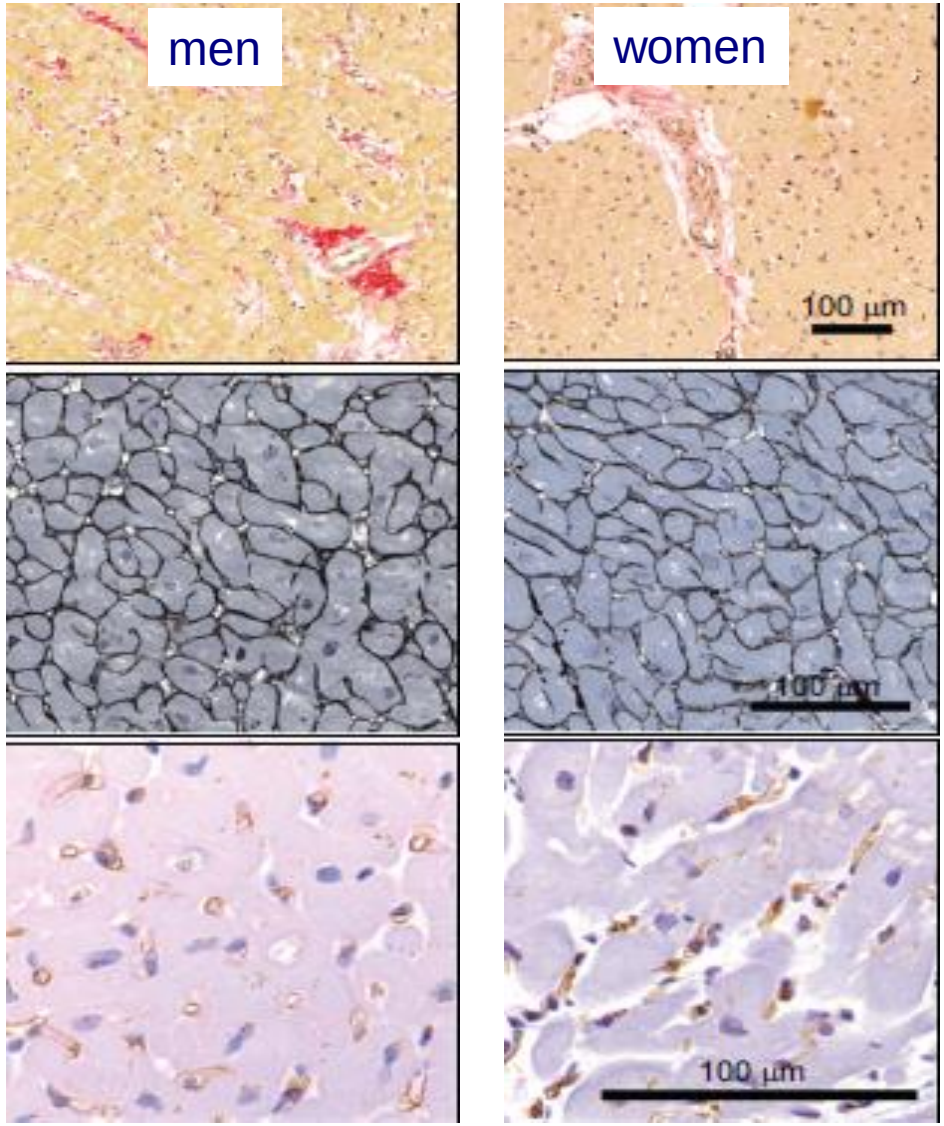
Sex differences in hypertension-related renal and cardiovascular diseases in Italy: the I-DEMAND study



Muiesan ML et al Journal of Hypertension 2012

Myocardial Structure in Men and Women

46 M, 11 F undergoing coronary artery bypass graft surgery
histological analysis of biopsies from nonischemic LV myocardium



Interstitial (↓W) and perivascular (M=W) fibrosis
Arteries size

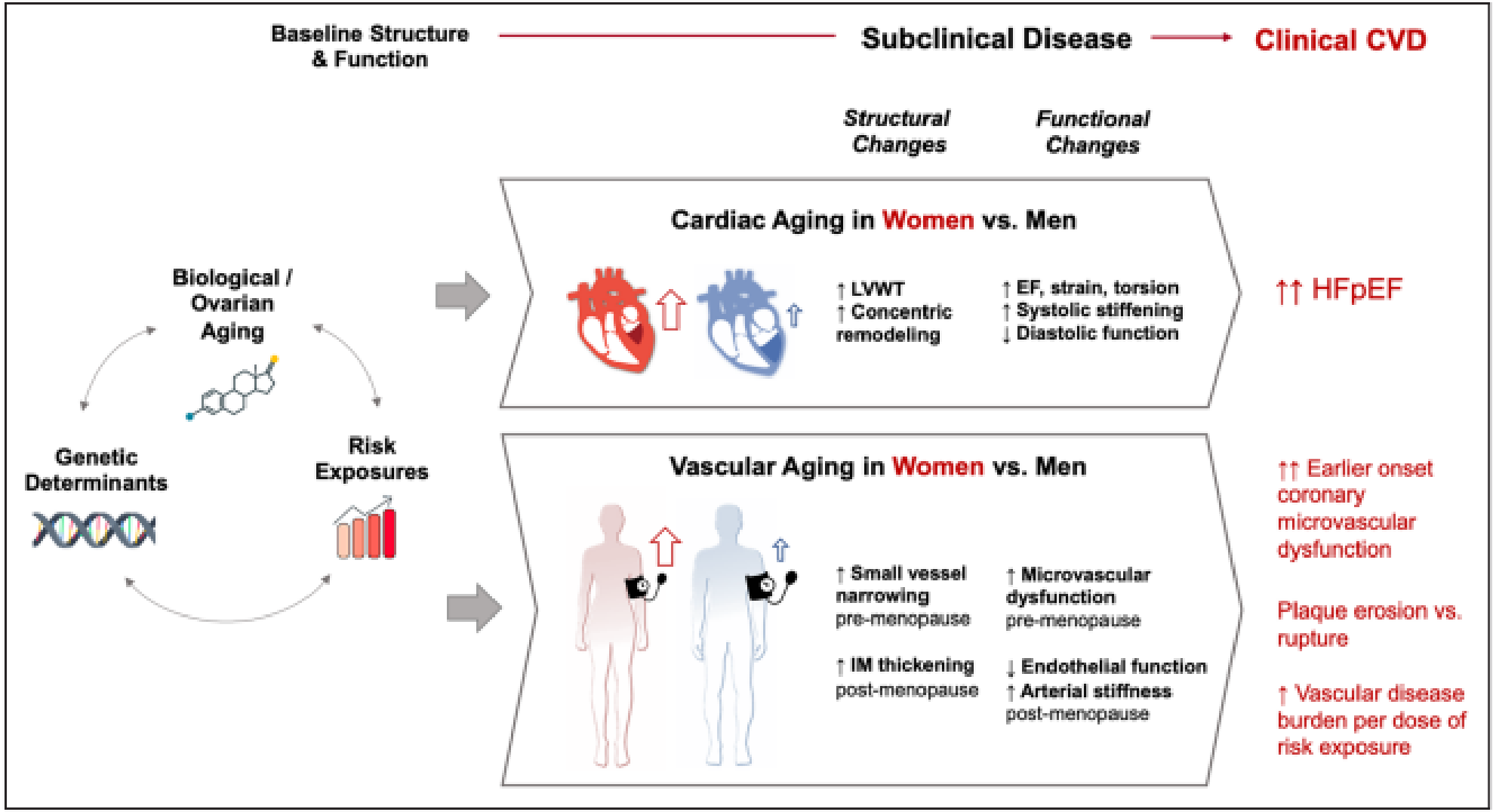
Cardiomyocites size,
Reticoline

Capillaries (CD31 positive)

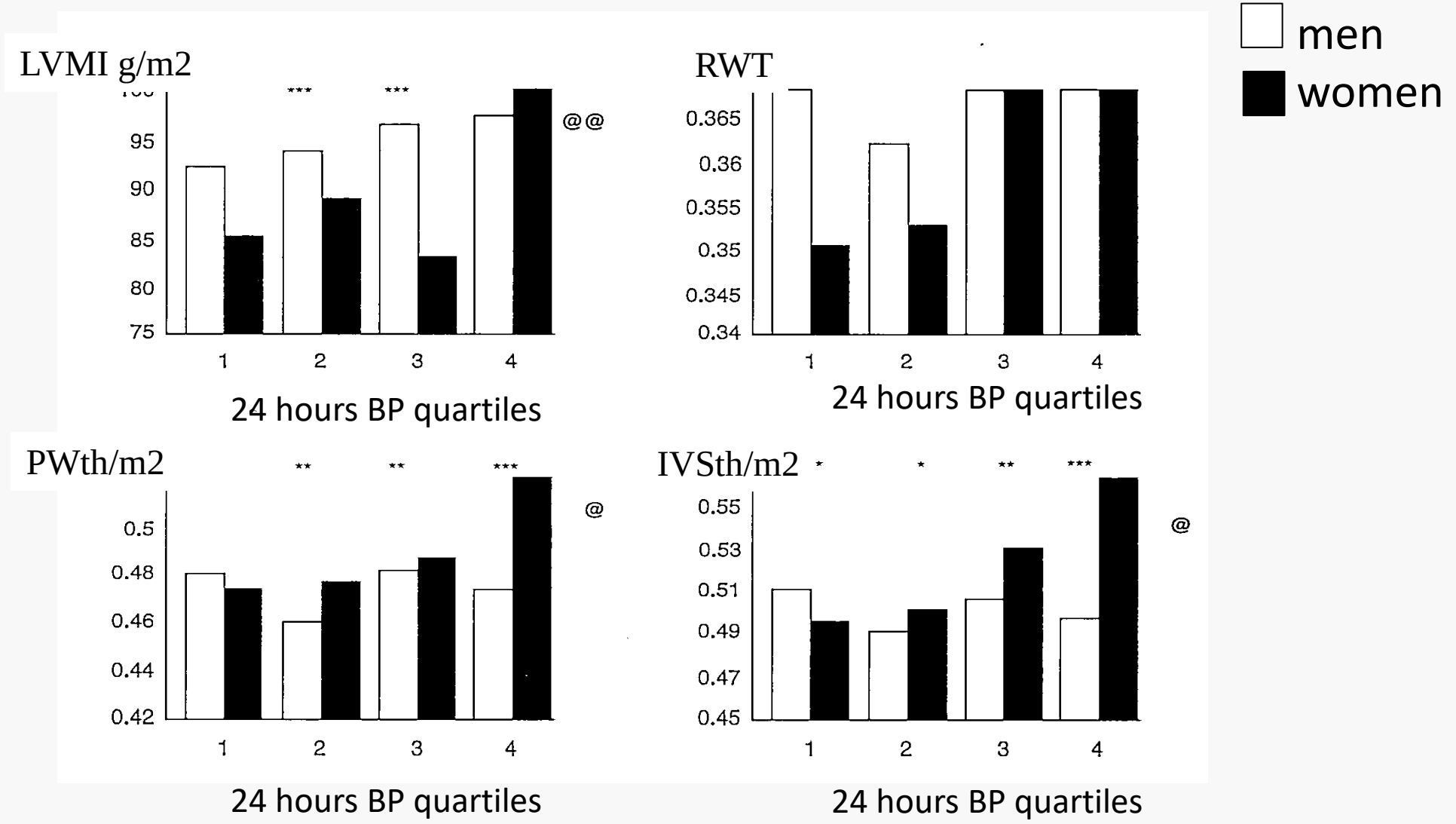
Arterioles area/circumference ratio
47% greater in women (*P* =0.012).

***Hypertension*. 2011;57:186-192.**

Cardiovascular aging phenotypes



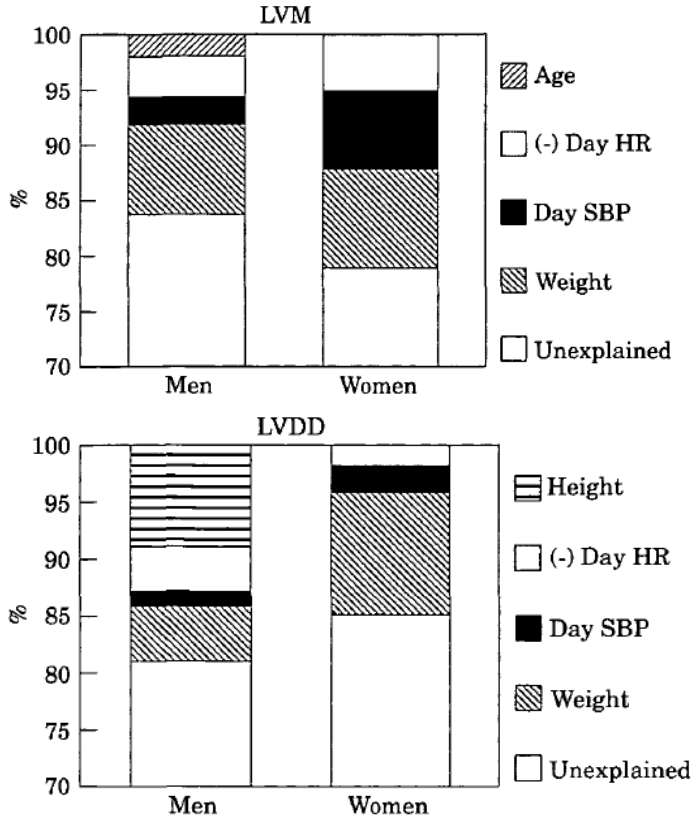
Target organ damage and ambulatory blood pressure in stage I hypertension. The HARVEST study.



Palatini P et al Blood Press Monit. 1997 Apr;2(2):79-88

Gender differences in LV size and function in young hypertensives

N=499 subjects 18-45-year-old with stage I hypertension (Harvest study)
377 men and 122 women. Mean age 33 ± 9 years
Office BP 146/94

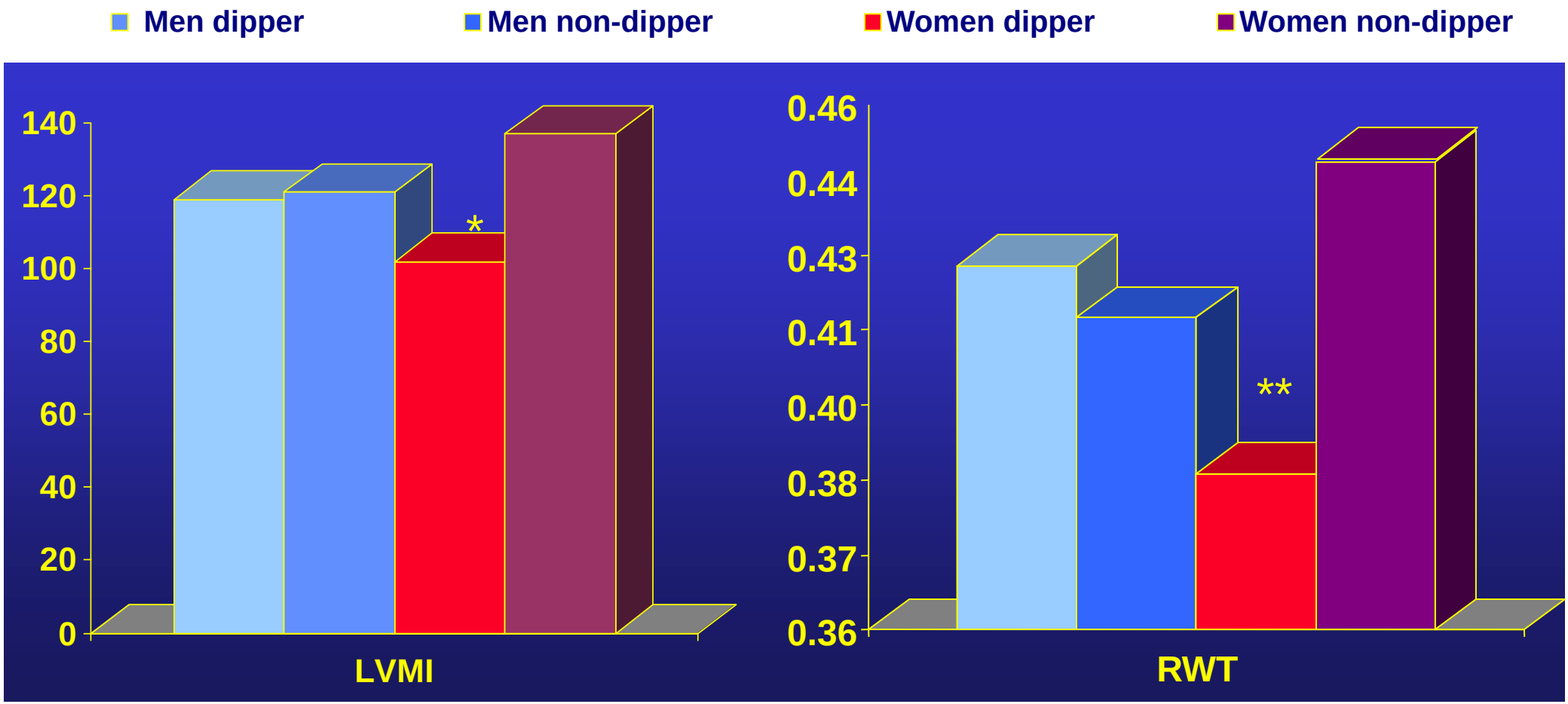


Correlation coefficients of indexes of LV structure and function by gender

	Day-time SBP		Day-time DBP	
	Men r	Women r	Men r	Women r
LVM	0·19***	0·27**	0·16**	0·16
RWT	0·005	0·17	0·01	0·20*
PWT	0·14**	0·32***	0·12*	0·22*
IVS	0·11*	0·29**	0·13*	0·26**
LVDD	0·16**	0·10	0·14**	0·02

Vriz O et al. Eur Heart J. 1997;18:664-670

Gender-specific cardiovascular adaptation due to circadian BP variations

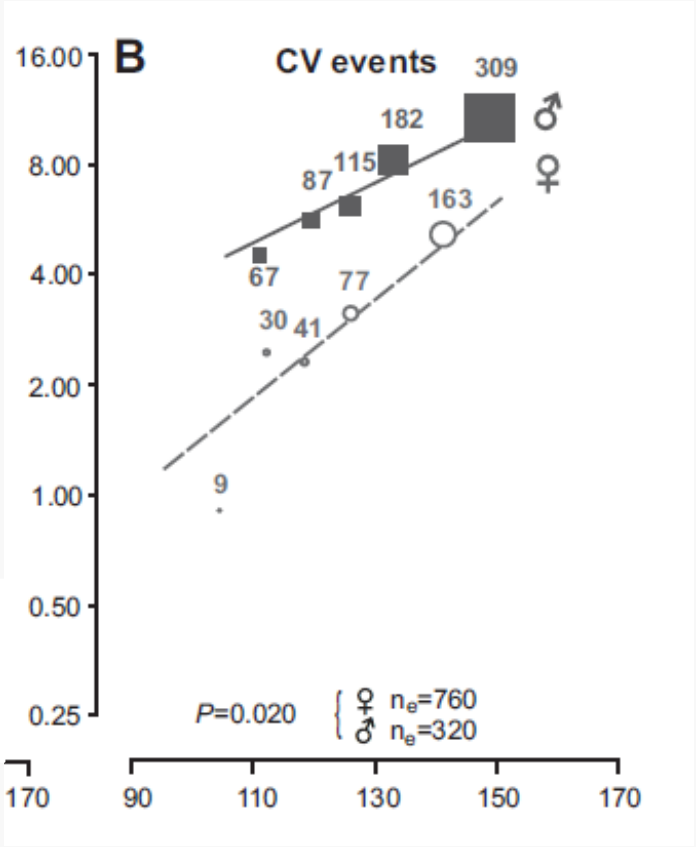


** p< 0.01 * p< 0.05 vs non dipper female

Schmieder et al AHJ, 1995

Ambulatory Blood Pressure Monitoring in 9357 Subjects From 11 Populations Highlights Missed Opportunities for Cardiovascular Prevention in Women

9357 subjects (age, 52.8 yrs; 47% women)
Women compared with men were at lower risk (HR for CV events 0.62 p<0.001)
However, **the relation of all events with 24-hour BP and with nighttime BP were steeper in women than in men**



"…consequently, ***per a 1-SD (13.4 mmHg) decrease, the proportion of potentially preventable events was higher in women than in men for all cardiovascular events (35.9% vs 24.2%)*** *in relation to 24-hour systolic BP…"*

IDACO Investigators, Hypertension 2011

Prevalence of LVH in hypertension:

Electrocardiographic studies

A sex-based analysis in 5 out of 26 studies (12084 patients) showed an average prevalence of LVH of 24% in men and 16% in women (odds ratio 1.38, 95% CI 0.91-2.09, *P*=0.11).

Echocardiographic studies

30 studies, including 37 700 untreated and treated patients (80.3% Caucasian, 52.4% men, 9.6% diabetics, 2.6% with CV disease) LVH prevalence was not different between women and men (range 37.9 -- 46.2 versus 36.0 --43.5%, respectively).

Cuspidi C et al J Hypertens and JJH 2012

Hazard ratios for CV events, according to sexes The Molisani study

	Women (N=10033)		Men (N=8297)		P for difference
	HR*	98%CI	HR*	98%CI	
Strain	5.23	0.72 to 38.0	5.33	1.30 to 21.8	0.95
Sokolov	3.17	0.42 to 24.21	1.61	0.40 to 6.52	0.42
Cornell (V)	1.31	0.66 to 2.59	4.00	1.26 to 12.66	0.12
Ra AVL	2.16	1.06 to 2.55	0.72	0.27 to 1.93	0.068
Cornell (P)	1.40	0.87 to 2.25	2.14	1.24 to 3.70	0.35
Any of them	1.61	1.05 to 2.48	9.97	3.04 to 32.74	0.50

*Adjusted for age, cigarette, hypertension, hypercholesterolemia, diabetes, income, education, occupational class, physical activity, BMI categories, including a term for interaction of the LVH indicator with sex

Muiesan ML et al, J Hypertens 2016

LVH associated CV risk in men and women

		All cause death		Cardiac Death	
		Men	Women	Men	Women
LV mass / height ^{2}	≥ 143 g/m ≥ 102 g/m	2.4	2.9	1	4.4 *
LV mass / height $^{2.7}$	≥ 50 g/m $^{2.7}$ ≥ 47 g/m $^{2.7}$	1.4	3.0	1	6.0 *
LV mass/ BSA	≥ 131 g/m ^{2} ≥ 100 g/m ^{2}	2.1	3.6	1.4	6.5 *
LV mass/ BSA	≥ 117 g/m ^{2} ≥ 104 g/m ^{2}	2.0	4.3	1.3	7.5 *

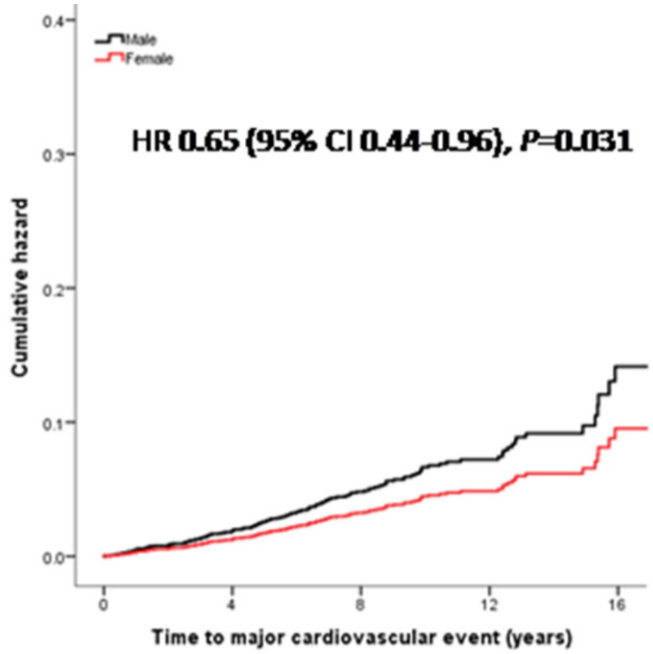
* sex-LVH interaction term

Liao Y et al, Circulation , 1995

Left ventricular hypertrophy offsets the sex difference in CV risk

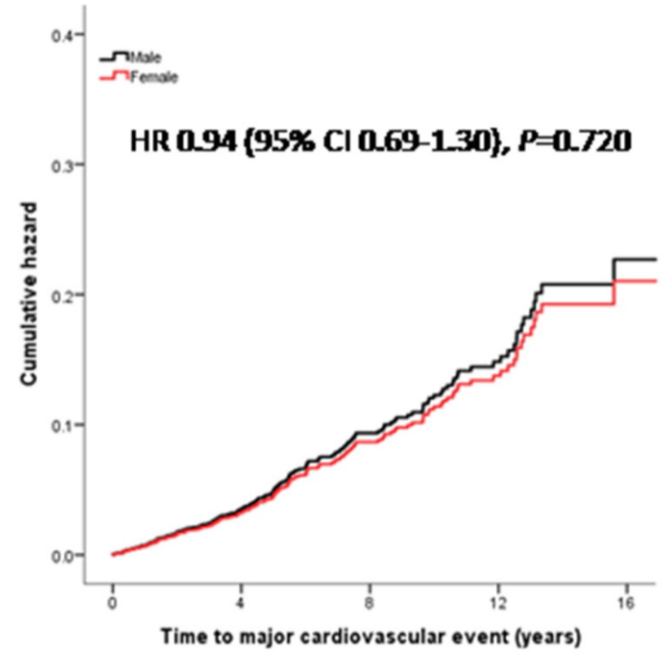
12,329 women and men with HTN and free from CV disease (Campania Salute Network)
FU: 4.1 years. MACE: combined acute coronary syndromes, stroke, hospitalization for HF and incident AF
Mean age 50 y, LVH=37%, obesity 17%

Without LVH



Patients at risk					
Women	3053	918	412	162	31
Men	4711	1463	716	317	64

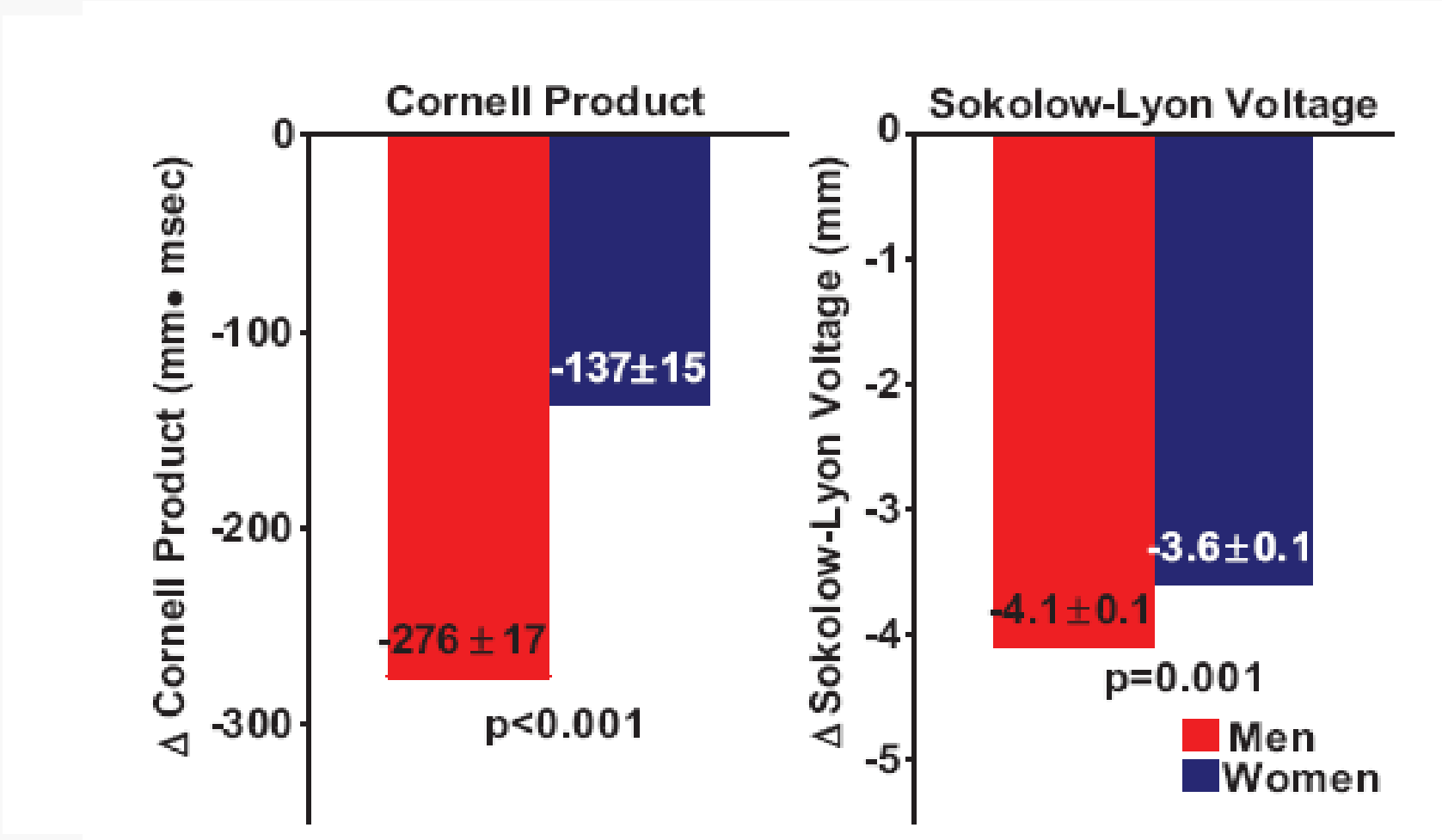
With LVH



Patients at risk					
Women	2339	645	307	119	24
Men	2226	727	332	144	27

Gerdts E et al, Int J Cardiol. 2018;258:257-261

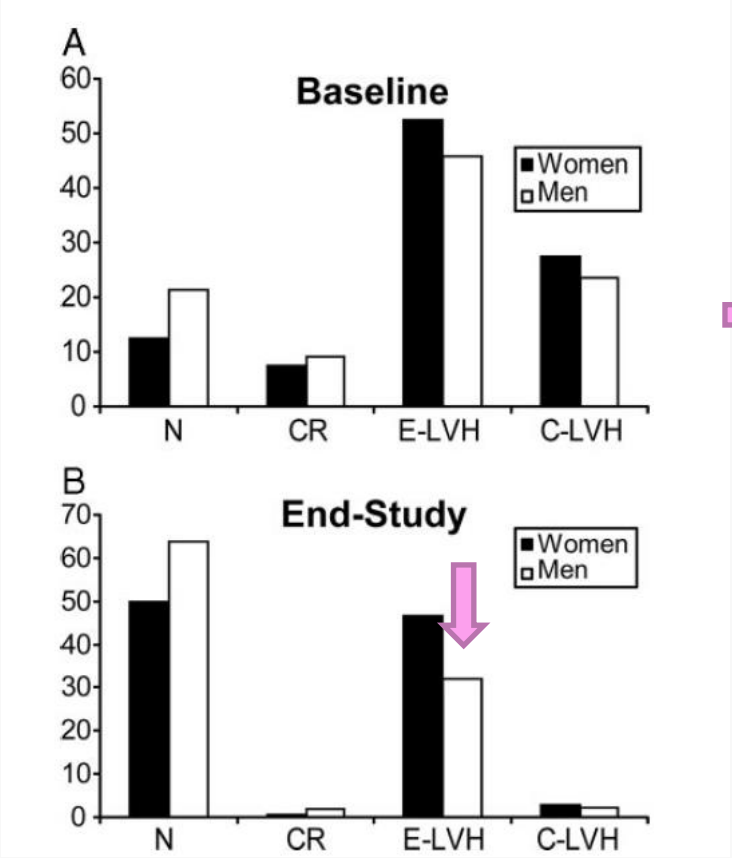
Gender Differences in Regression of Electrocardiographic LVH During Antihypertensive Therapy



Okin et al Hypertension. 2008;52:100-106.

Gender differences in LV mass changes in response to antihypertensive treatment

N= 863 hypertensive patients with electrocardiographic LVH
FU: 4.8 years. LVH by EchoCG as LVM ≥ 46.7 g/m$^{2.7}$(W) and LVM ≥ 49.2 g/m$^{2.7}$ (M)

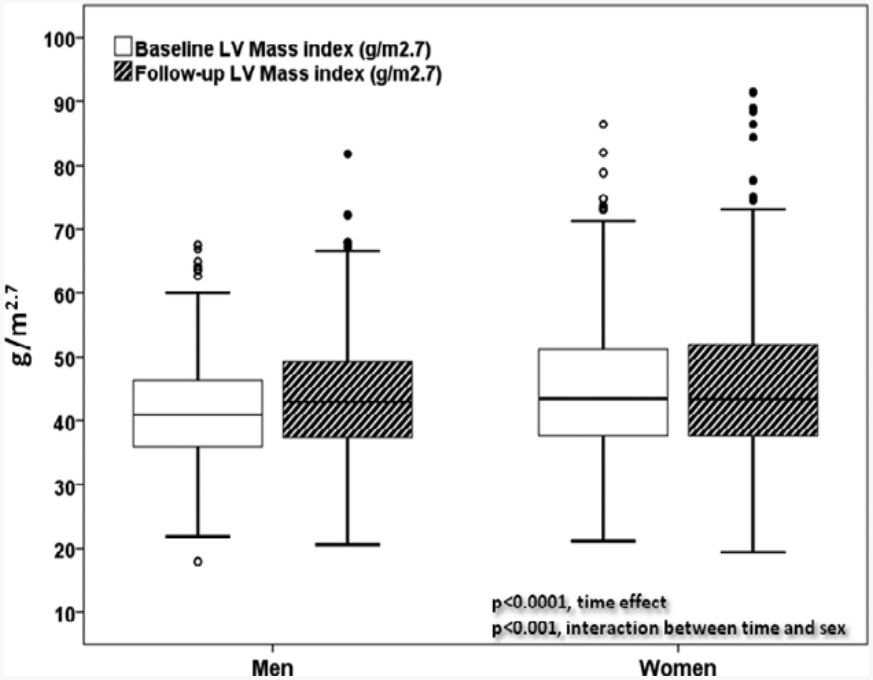


Predictors and Covariates of End-Study LV Hypertrophy

Variable	OR	95% CIs	*P*
Female gender	1.61	1.16 to 2.26	0.005
Age, 1 SD	1.35	1.12 to 1.61	0.001
Baseline LV hypertrophy	7.38	4.46 to 12.23	<0.0001
End-study pulse pressure, 1 SD	1.26	1.06 to 1.51	0.009
End-study body mass index, 1 SD	1.99	1.65 to 2.70	<0.001
Lower end-study LV EF, 1 SD	1.39	1.18 to 1.64	<0.0001
End-study mitral regurgitation	1.49	1.06 to 2.10	0.022
End-study aortic regurgitation	1.77	1.61 to 2.70	0.008

Gerdts E et al. Hypertension 2008;51:1109-1114

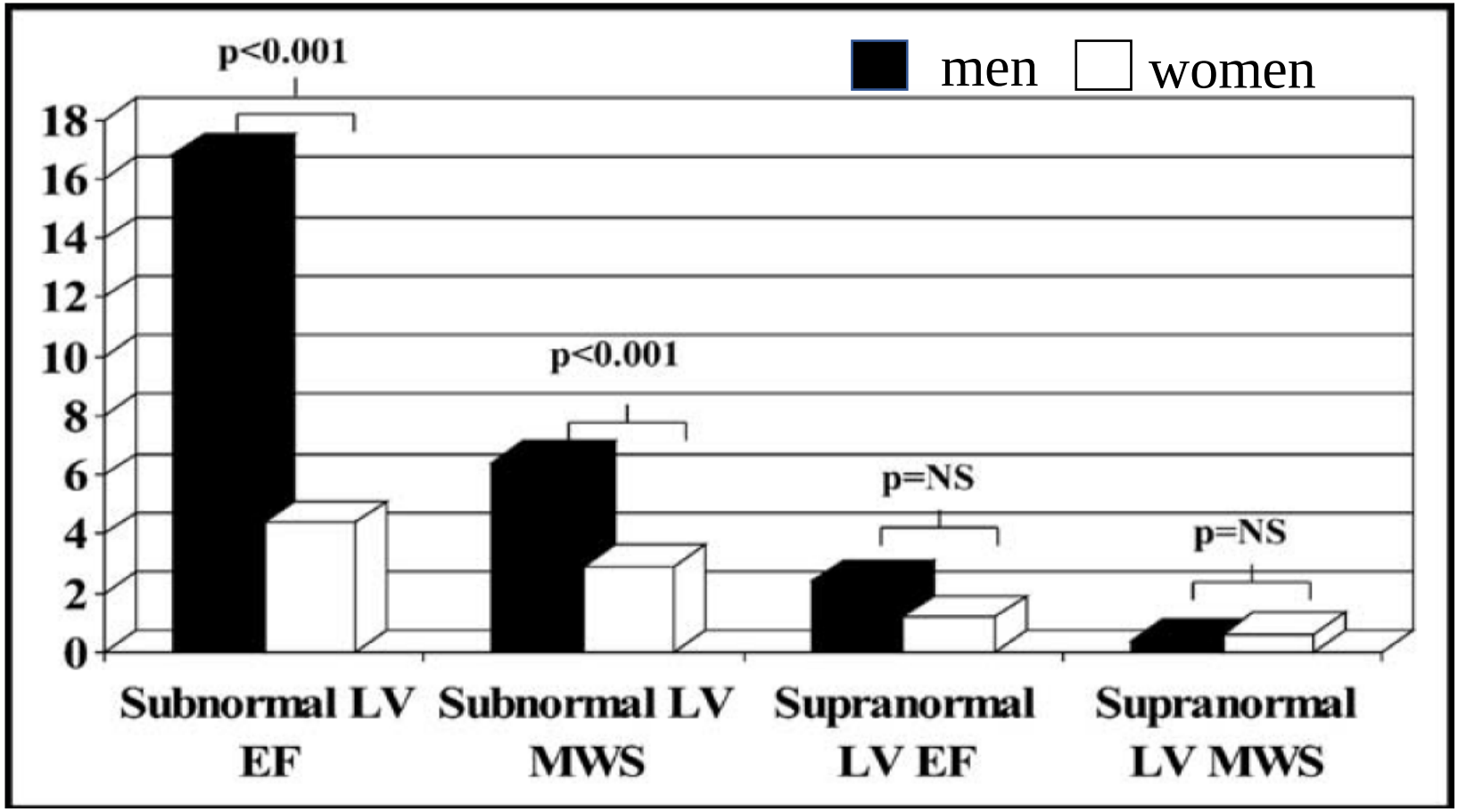
Lack of Reduction of Left Ventricular Mass in Treated Hypertension: The Strong Heart Study



In multivariable logistic regression,
lack of decrease in LVMi was associated with
-initially higher BMI
-urinary albumin/creatinine ratio
-older age
-female gender
-change in BP over time of follow up

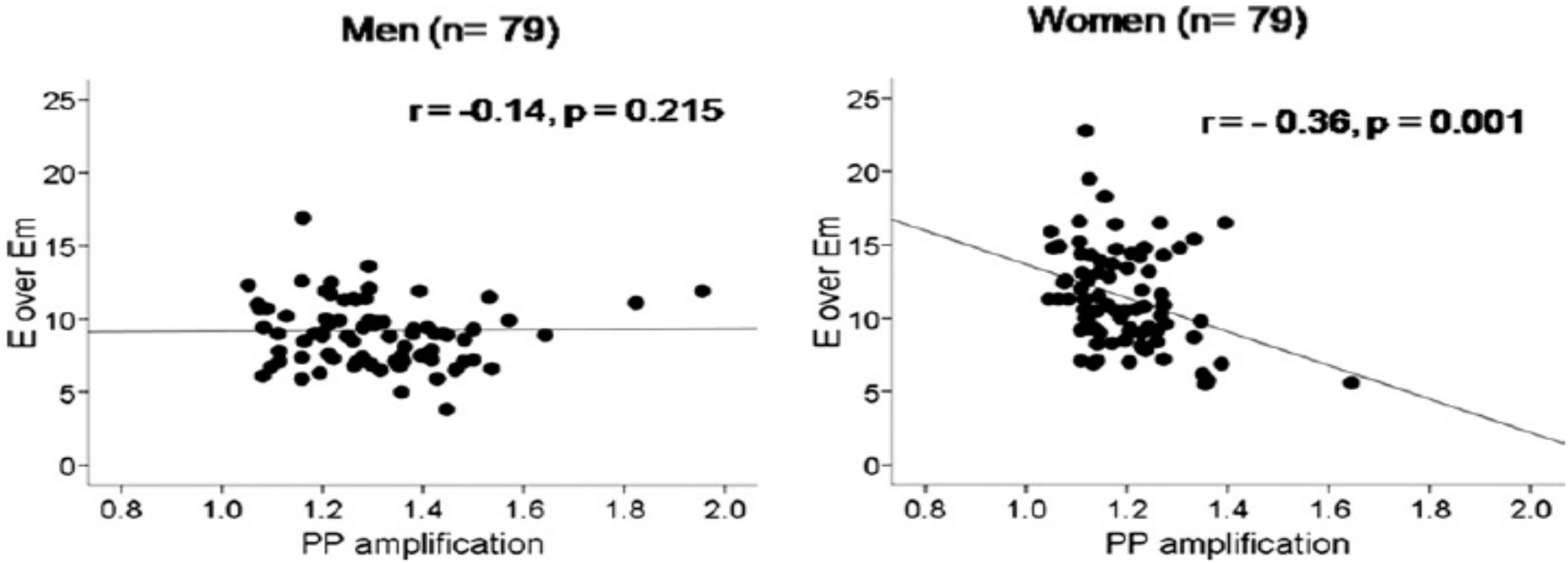
de Simone et al J Am Heart Ass, 2013

Hypertensive women have higher systolic function Strong Heart Study



Bella J et al Am J Cardiol. 2006;98(6):834-7

Central Hemodynamics and Diastolic Function



Shim et al ; JACC 2011

Left atrial volume indexed for height^2 is a new sensitive marker for subclinical cardiac organ damage in female hypertensive patients

Lorenzo Airale[1] · Anna Paini[2] · Eugenia Ianniello[3] · Costantino Mancusi[4] · Antonella Moreo[5] · Gaetano Vaudo[6] · Eleonora Avenatti[1] · Massimo Salvetti[2] · Stefano Bacchelli[3] · Raffaele Izzo[4] · Paola Sormani[5] · Alessio Arrivi[6] · Maria Lorenza Muiesan[2] · Daniela Degli Esposti[3] · Cristina Giannattasio[5] · Giacomo Pucci[6] · Nicola De Luca[3] · Alberto Milan[1] · on behalf of the Working Group on Heart and Hypertension of the Italian Society of Hypertension

Variable	Population ($n = 441$)	Male ($n = 229$)	Female ($n = 212$)	p
Left ventricle				
LVMI (g/m^2)	93.8 ± 26.4	99.8 ± 27.9	87.3 ± 23.1	**<0.001**
LVH	122 (27.7)	54 (23.6)	68 (32.1)	**0.046**
-Eccentric	35 (7.9)	13 (5.7)	22 (10.4)	0.068
-Concentric	87 (19.7)	41 (17.9)	46 (21.7)	0.317
RWT	0.42 ± 0.08	0.42 ± 0.09	0.42 ± 0.08	0.449
EF (%)	63.0 ± 7.8	61.7 ± 8.0	64.3 ± 7.4	**<0.001**
Diastolic function				
E/A	1.1 ± 0.6	1.0 ± 0.4	1.1 ± 0.8	0.084
Septal Em/Etdi	10.9 ± 4.3	10.4 ± 4.6	11.5 ± 3.9	**0.009**
Lateral Em/ Etdi (402)	8.4 ± 3.9	7.8 ± 3.1	8.9 ± 4.5	**0.003**
Mean Em/Etdi (402)	9.3 ± 3.4	8.8 ± 3.2	9.8 ± 3.4	**0.002**
Left Atrium				
LAV_{h2} (ml/m^2)	19.0 ± 7.5	18.9 ± 7.2	19.2 ± 7.8	0.643
LAe_{h2} n (%)	223 (50.6)	98 (42.8)	125 (59.0)	**0.001**
LAV_{BSA} (ml/m^2)	28.6 ± 10.8	28.6 ± 10.7	28.5 ± 10.9	0.877
LAe_{BSA} n (%)	103 (23.4)	53 (23.1)	50 (23.6)	0.912

Hypertension Research (2021) 44:692–699

Left atrial volume indexed for height^2 is a new sensitive marker for subclinical cardiac organ damage in female hypertensive patients

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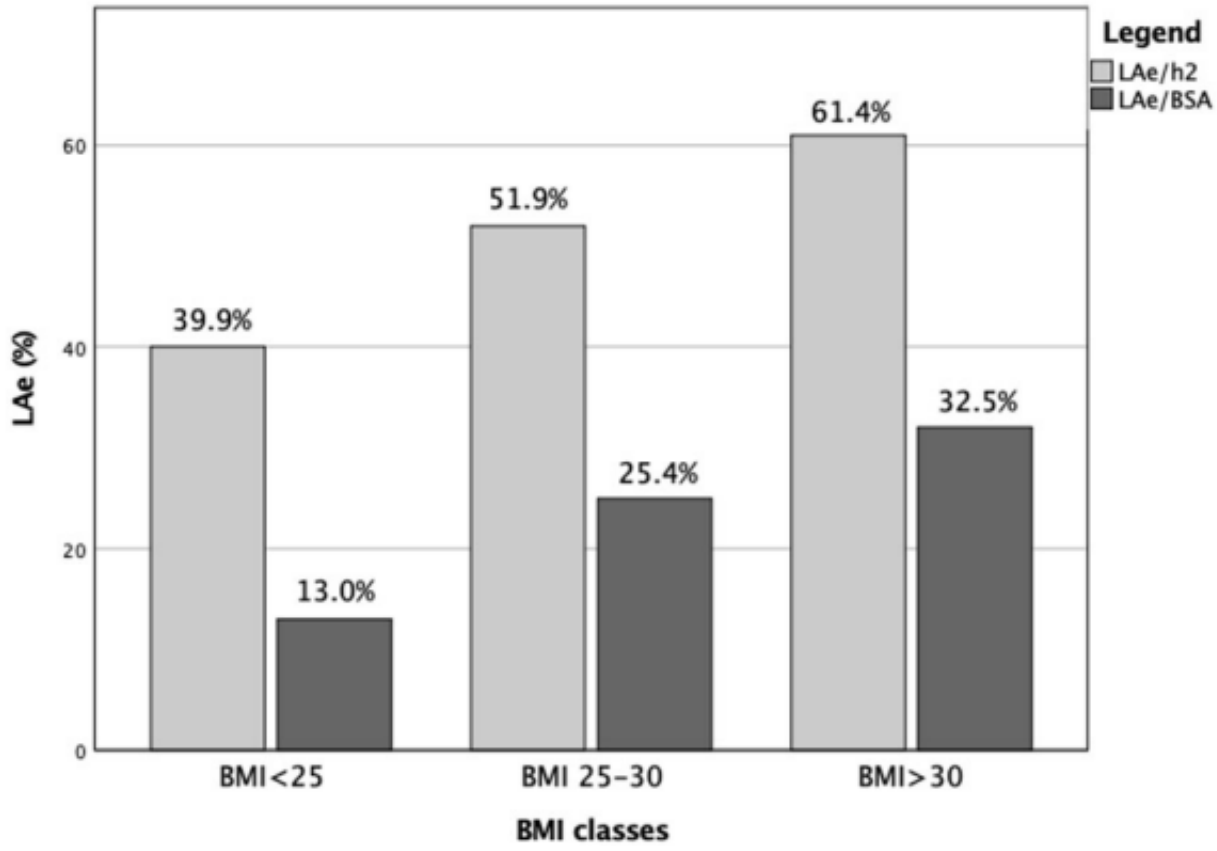

Hypertension Research (2021) 44:692–699

Left atrial volume indexed for height^2 is a new sensitive marker for subclinical cardiac organ damage in female hypertensive patients

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Variable	LA dilatation			*p*
	Norm ($n = 218$)	DilH ($n = 120$)	DilHB ($n = 103$)	
Age (years)	54.8 ± 12.8*‡	63.8 ± 14.5	67.4 ± 15.5	**<0.001**
Gender (male)	131 (60.1)*	45 (37.5)†	53 (51.5)	**<0.001**
Left ventricle				
LVMI (g/m^2)	85.8 ± 20.2*‡	93.7 ± 23.0†	110.0 ± 33.5	**<0.001**
LVH	30 (13.8)*‡	41 (34.2)†	51 (49.5)	**<0.001**
-Eccentric	6 (2.75)*‡	41 (34.2)	16 (15.5)	**<0.001**
-Concentric	24 (11.0)*‡	28 (23.3)	35 (34.0)	**<0.001**
RWT*	0.41 ± 0.08‡	0.42 ± 0.09	0.44 ± 0.09	**0.010**
EF (%)	63.6 ± 7.18	63.2 ± 7.62	61.4 ± 9.15	0.067
Diastolic function				
E/A	1.05 ± 0.51	1.01 ± 0.57	1.09 ± 0.95	0.662
Septal E/e′	9.49 ± 2.89*‡	11.4 ± 3.99†	13.3 ± 5.65	**<0.001**
Lateral E/e′	7.02 ± 2.11*‡	9.30 ± 5.27	10.0 ± 3.82	**<0.001**
Mean E/e′	7.93 ± 2.15*‡	9.93 ± 3.51†	11.2 ± 3.95	**<0.001**

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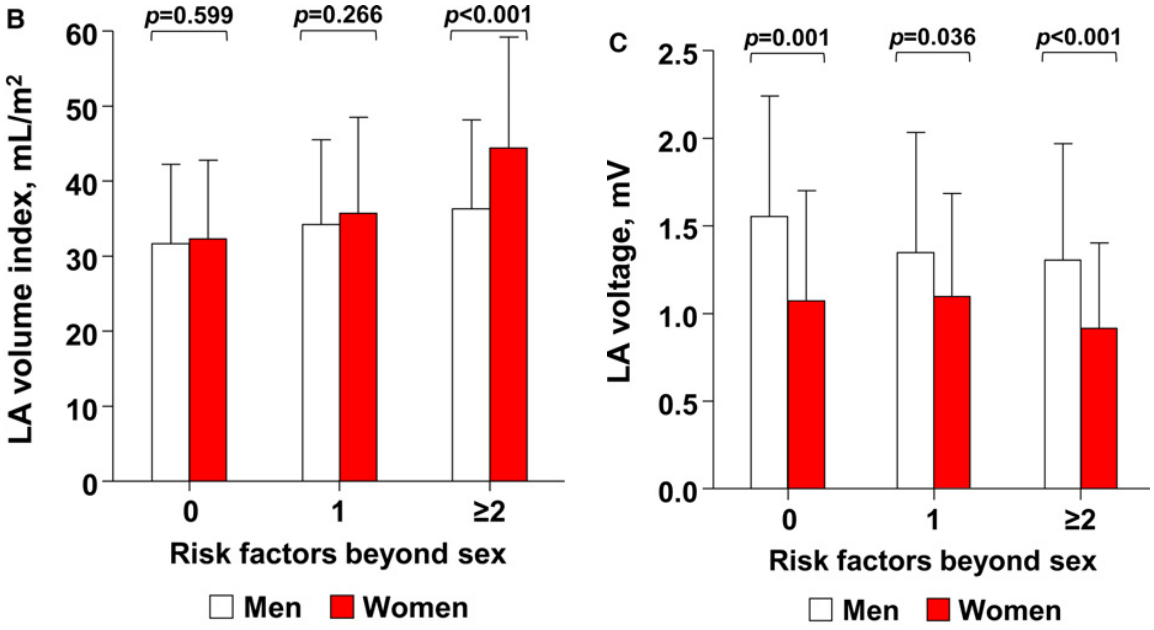
Left Atrial Remodeling and stroke risk in hypertensive women vs men

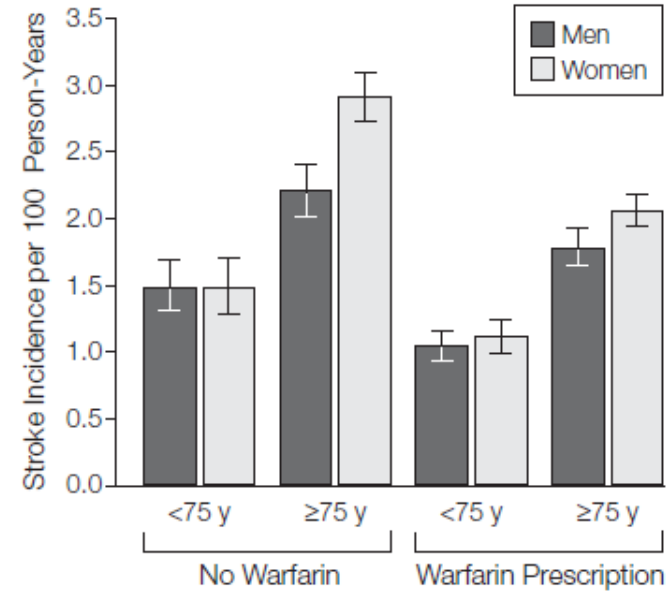
N= 579 AF patients (216 women, matched with 363 men for CV risk factors and diseases) undergoing AF catheter ablation
Mean age 61 years old. , 70.1%

Electroanatomical remodelling

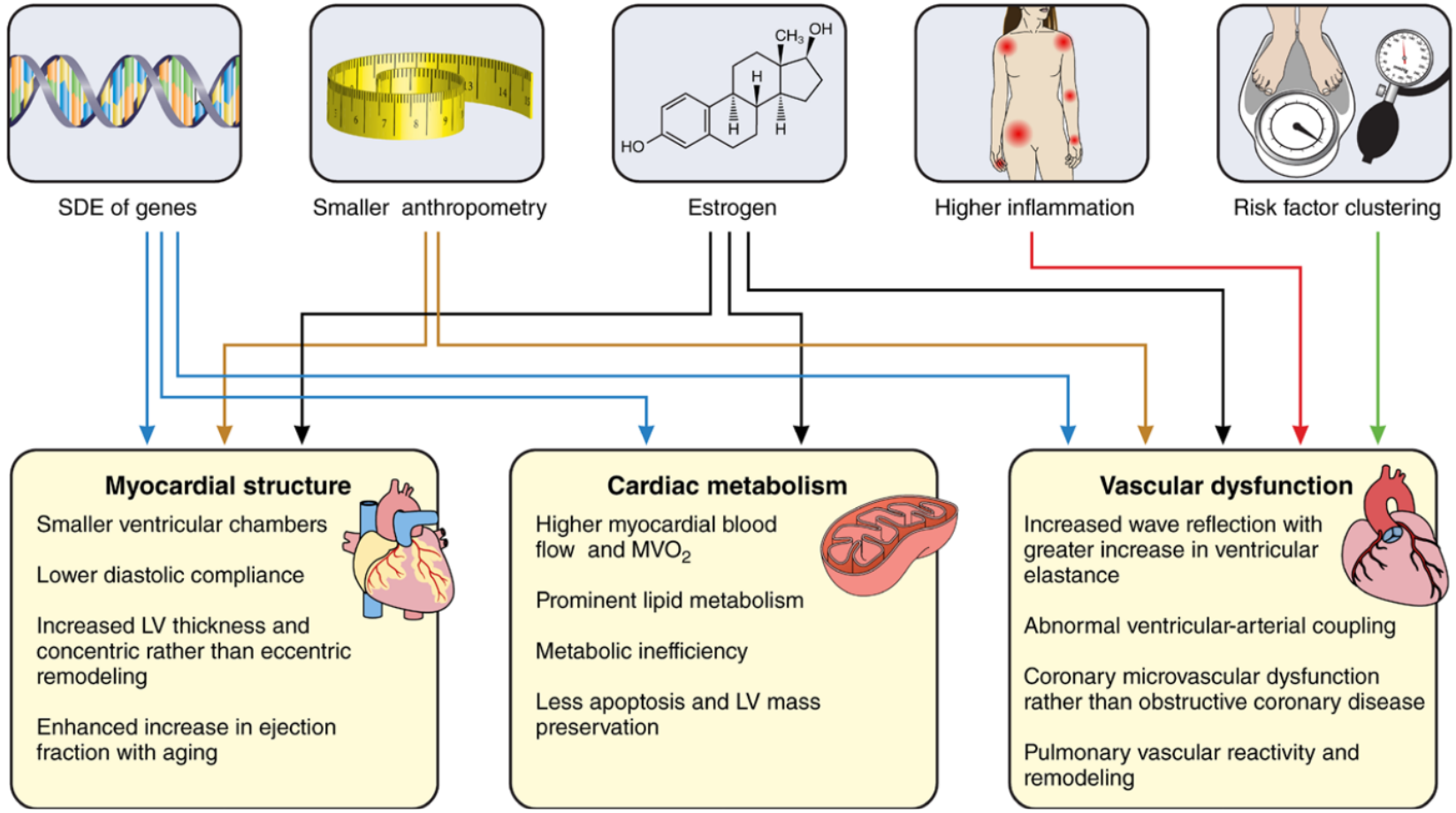


Yu HT et al, J Am Heart Assoc. 2016;5:e003361

Stroke risk



Avgil Tsadok M et al. JAMA. 2012;307:1952-1958



Beale AL et al, Circulation. 2018;138:198-205