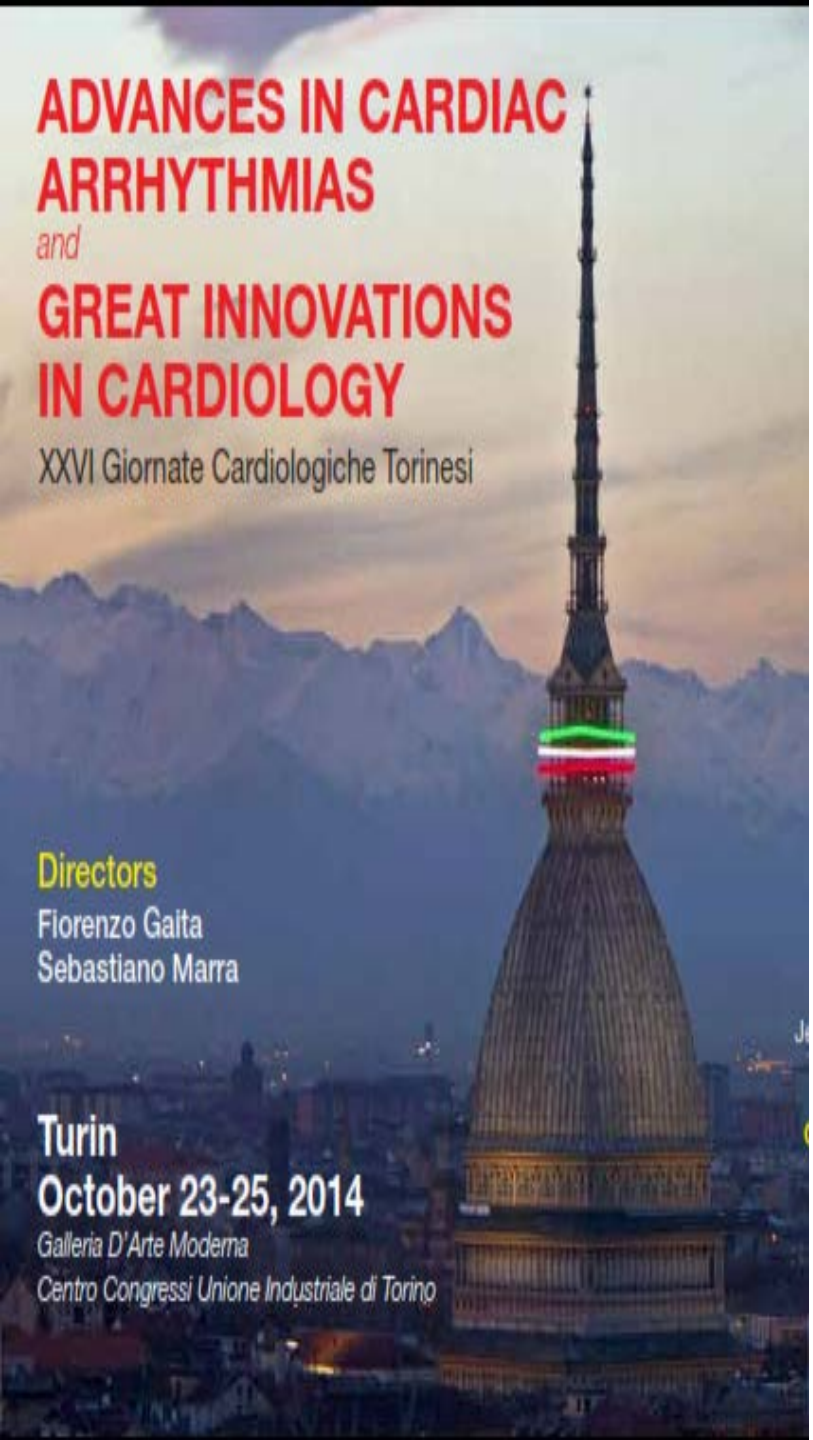


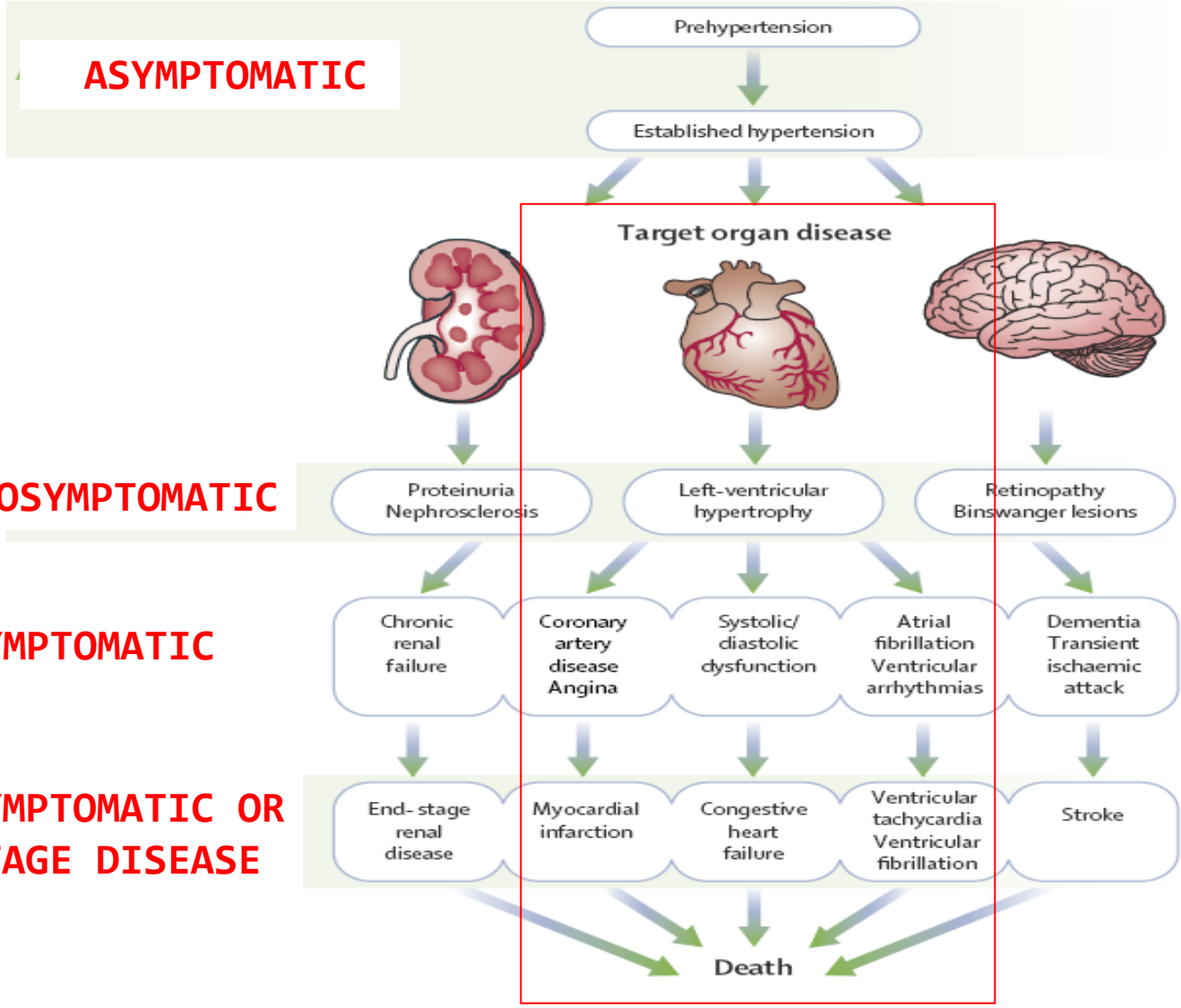
Università degli Studi di Torino
Dipartimento di Scienze Mediche
AO Citta' Salute e Scienza di Torino
SCU Medicina Interna, Centro Ipertensione Arteriosa
Torino

Hypertension, Left Ventricular Hypertrofia and Cardiomiopathy

Franco Veglio

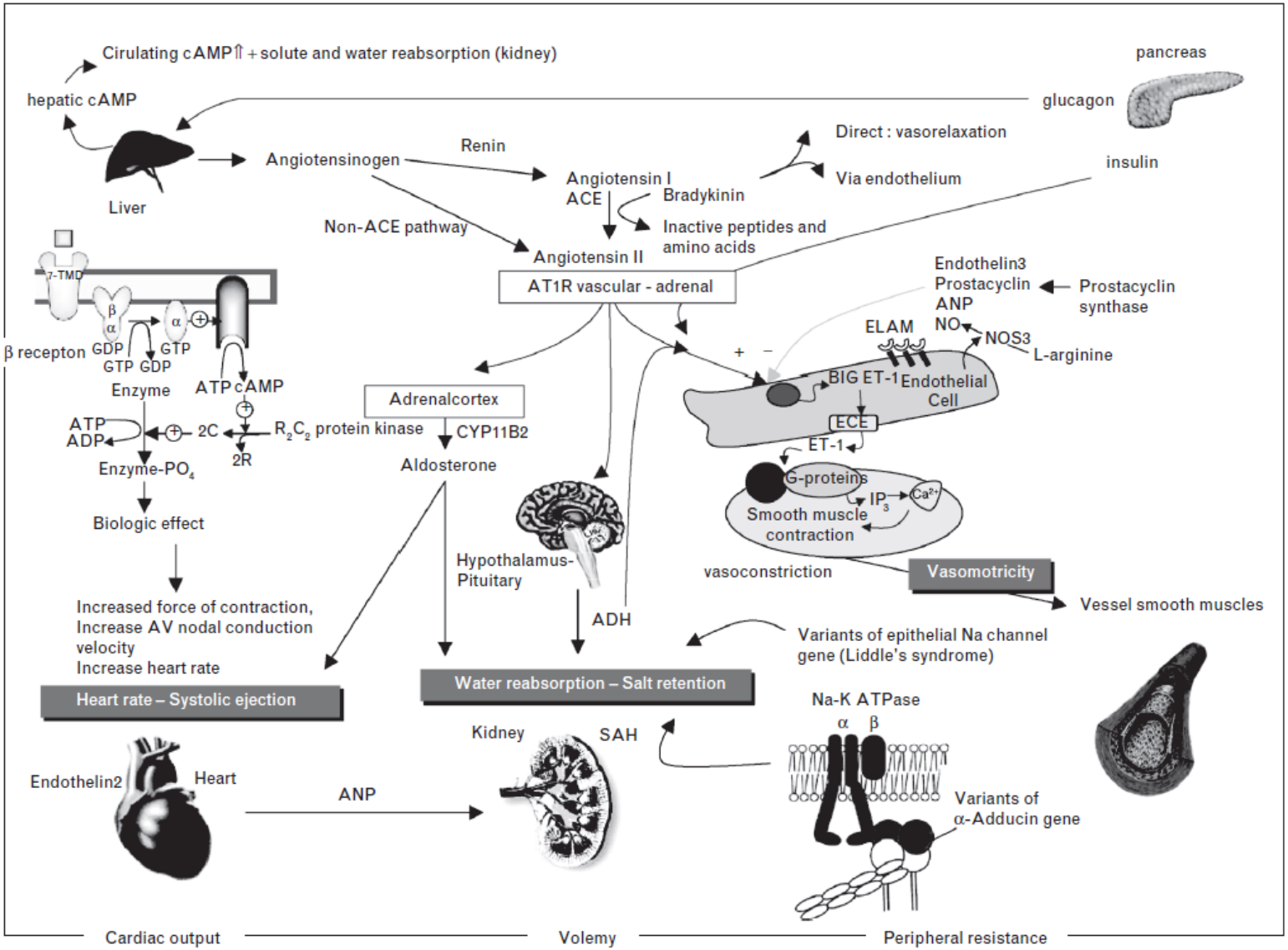
NO CONFLICTS OF INTEREST

TIMING HYPERTENSIVE DISEASE



Messerli, Lancet 2007

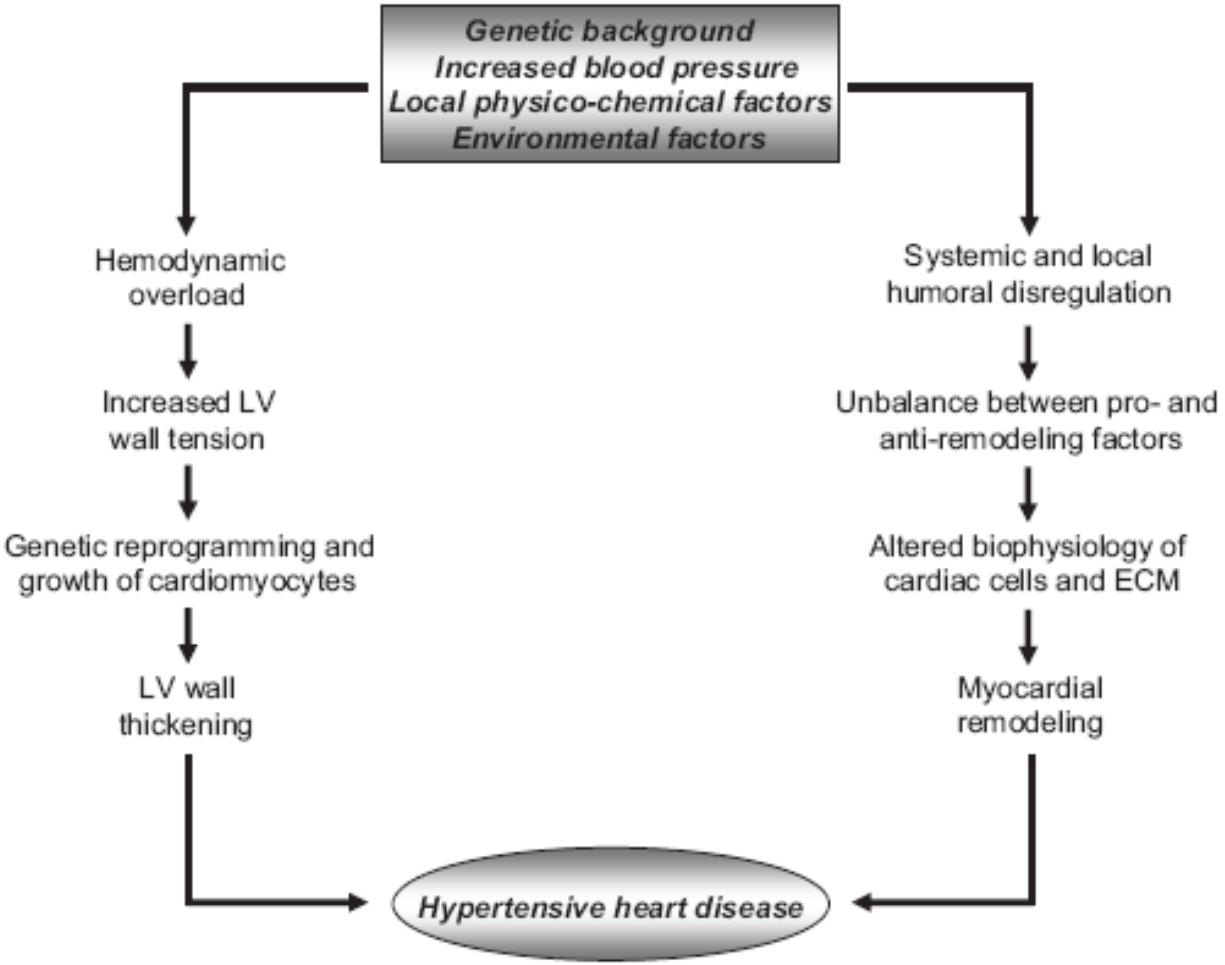
Multifactorial origin of Essential Hypertension



BP = CO x TPR

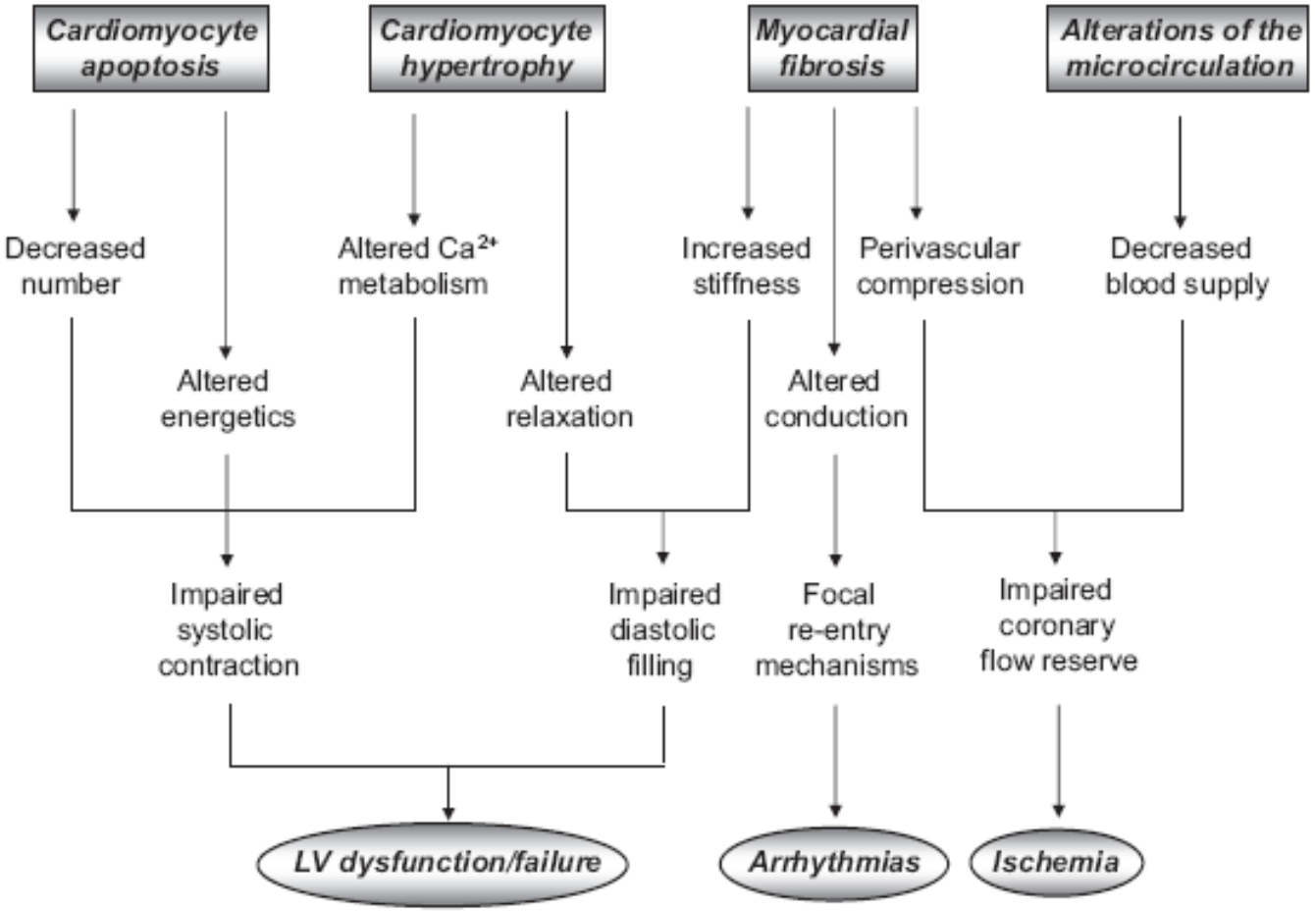
Kelly, J Hypertens 2012

Hypertensive Heart Disease



Díez, Hypertension 2010

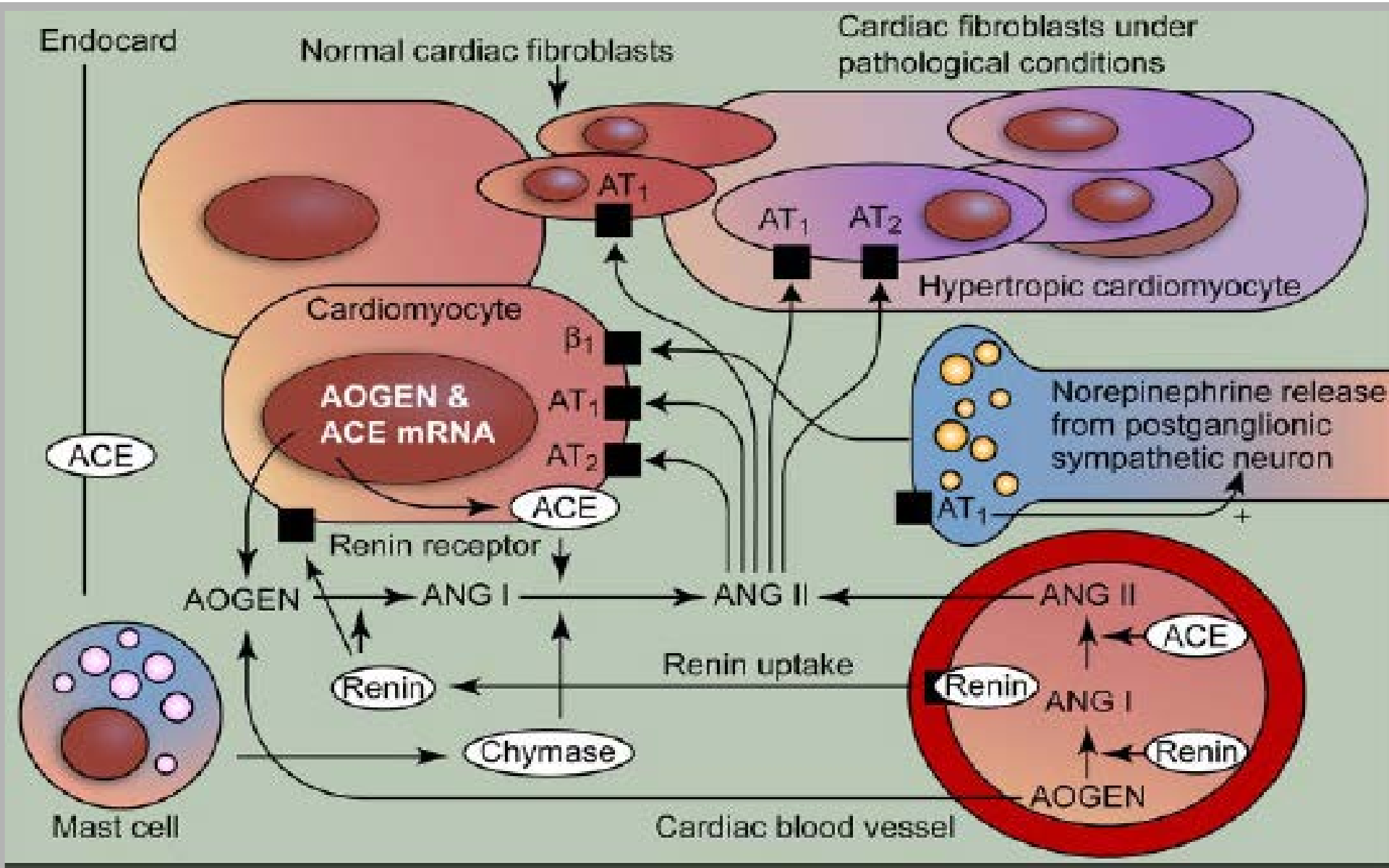
Hypertensive Heart Disease



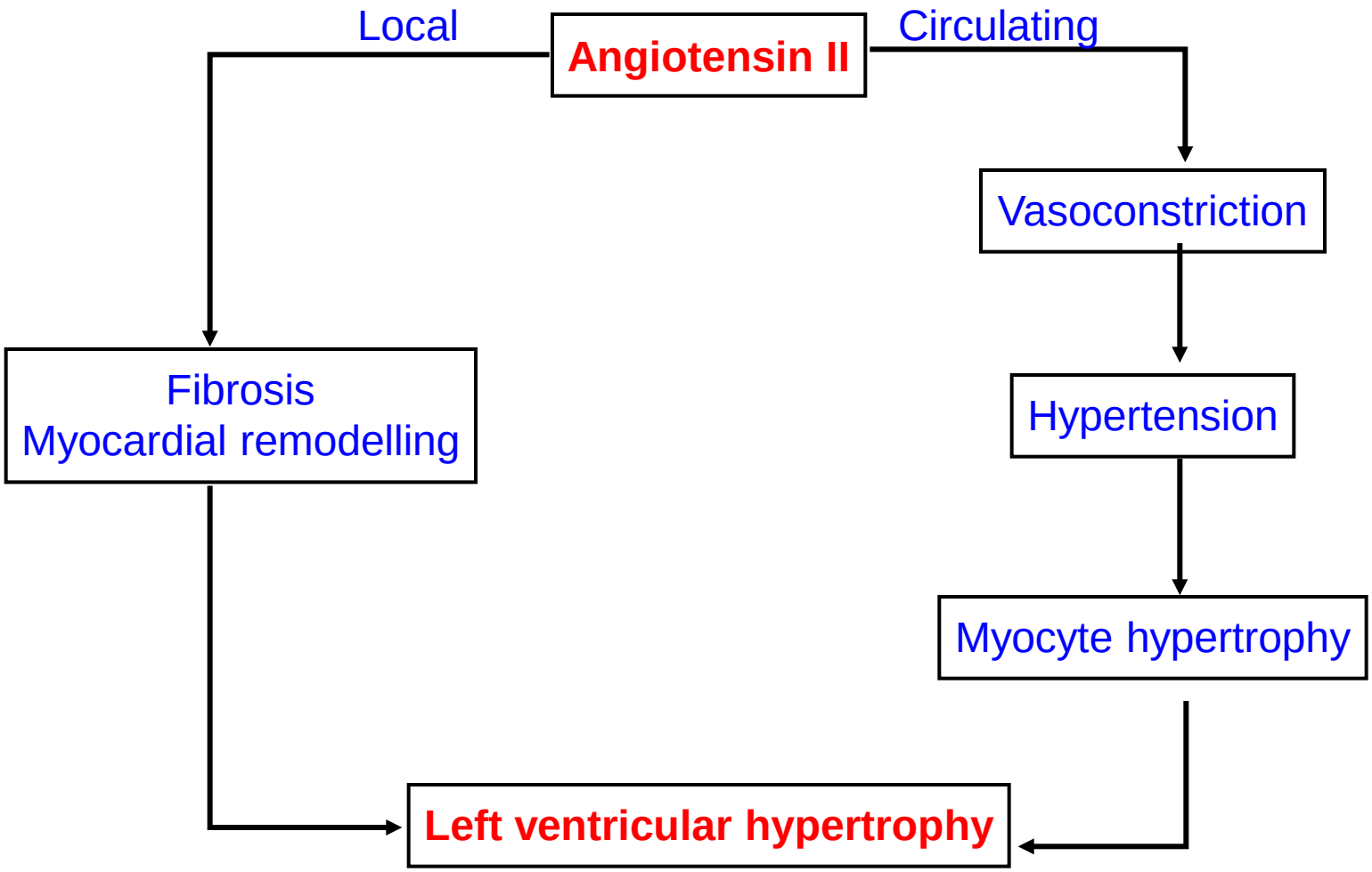
Díez, Hypertension 2010

RAS & HEART

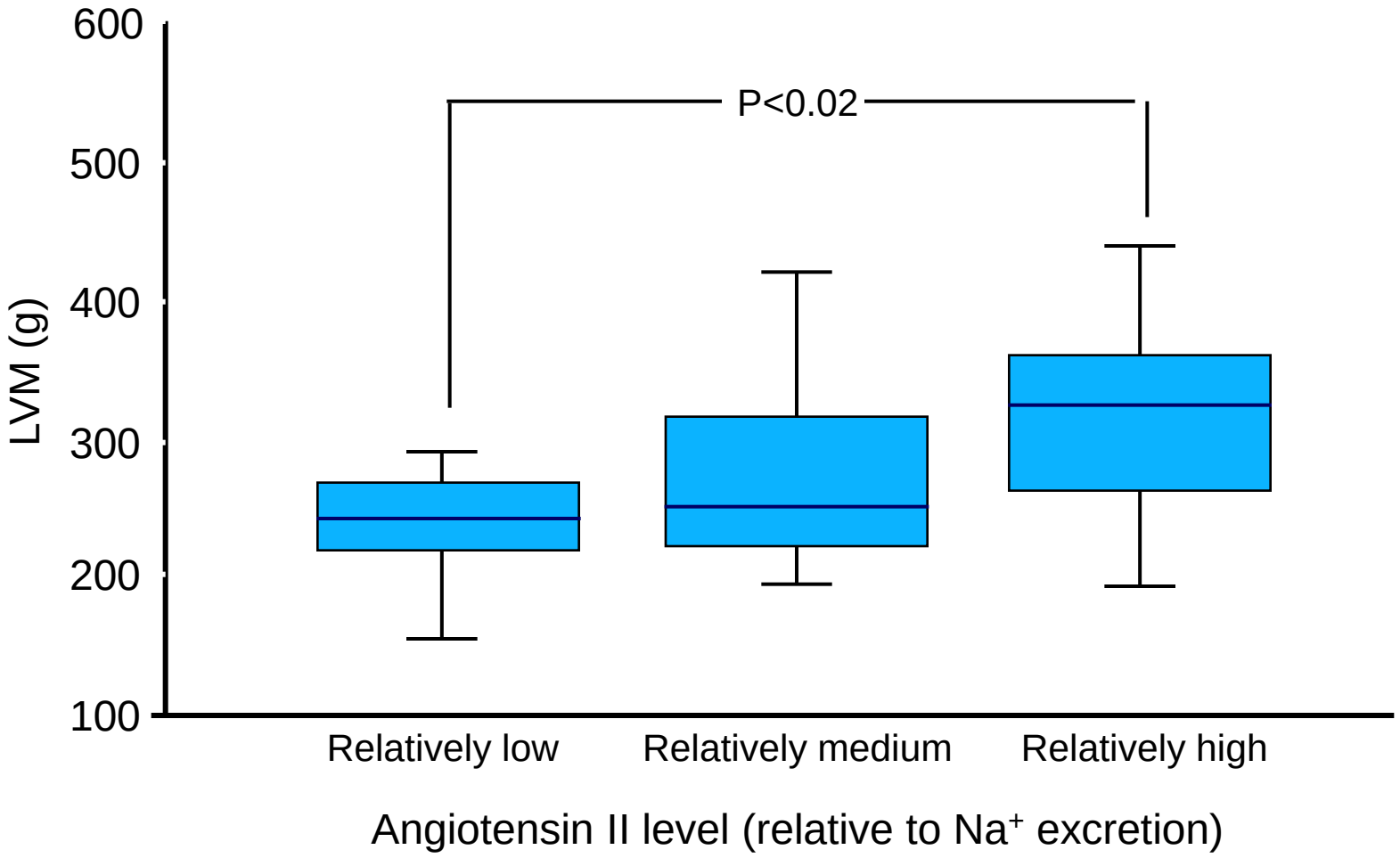
Paul, *Physiol Rev* 2006



Angiotensin II and the pathophysiology of LVH

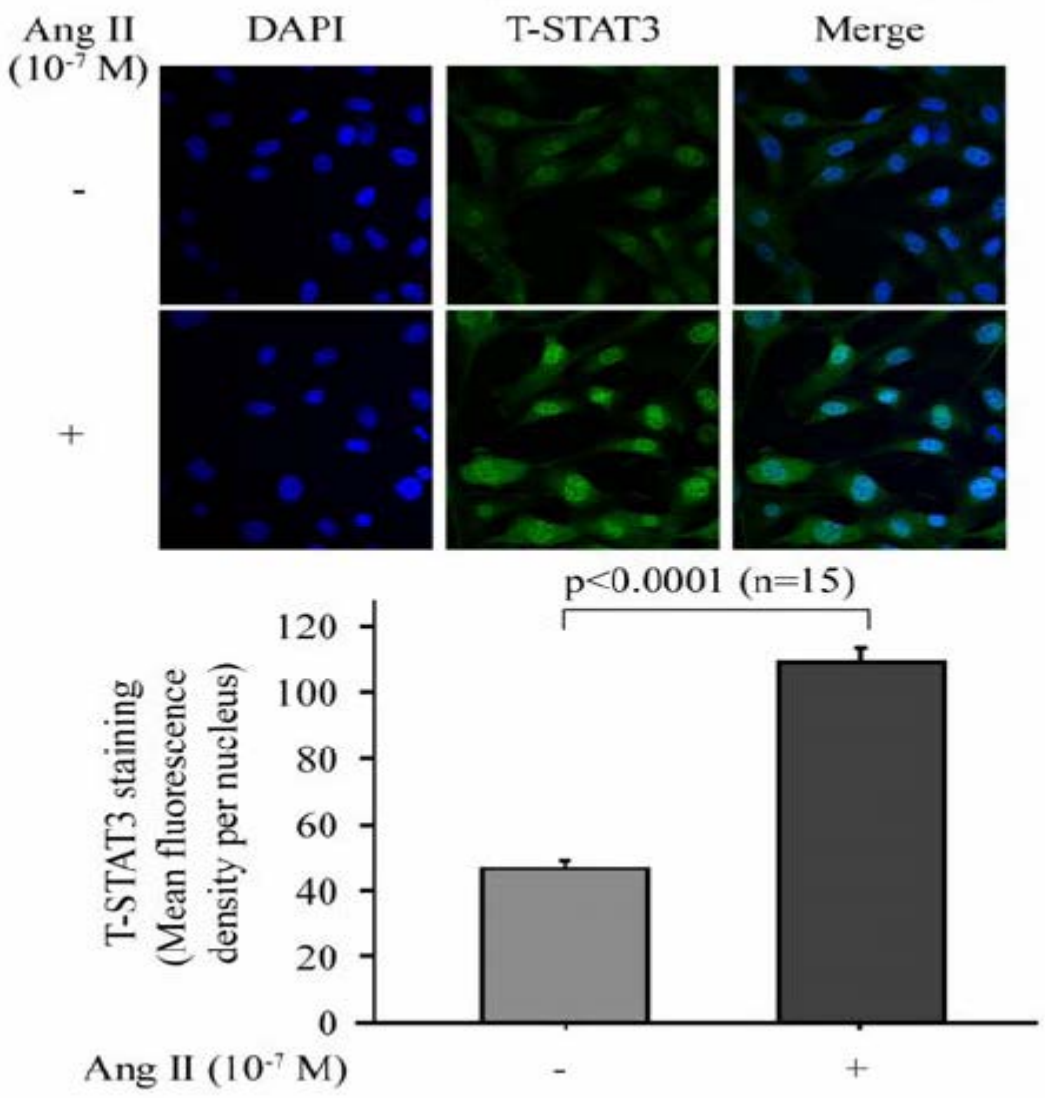


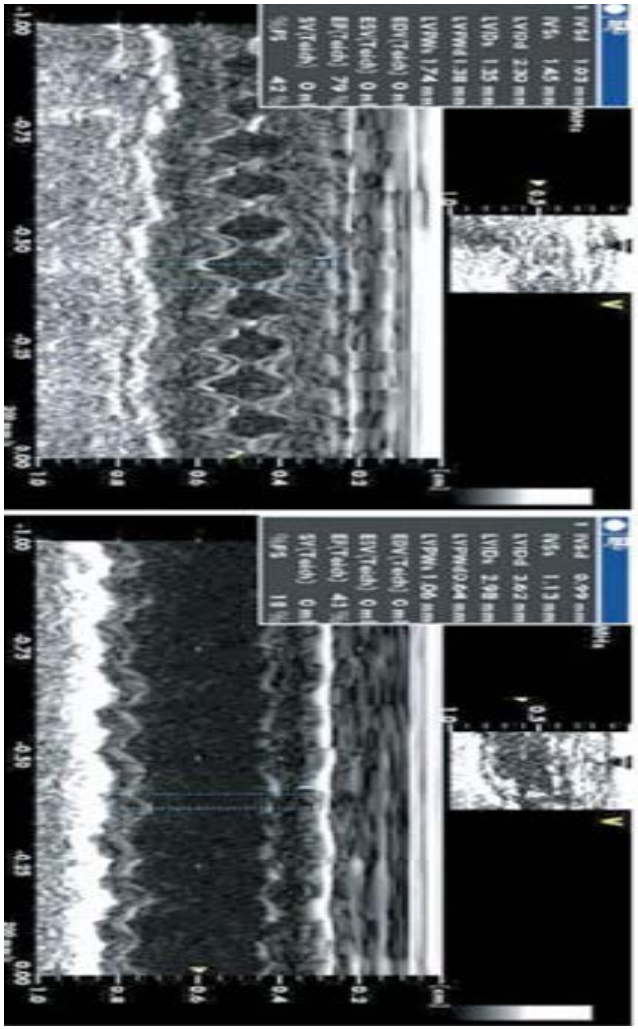
Angiotensin II levels correlate with LVM in hypertensive patients



Schmieder et al. *Circulation* 1996;94:1304–1309

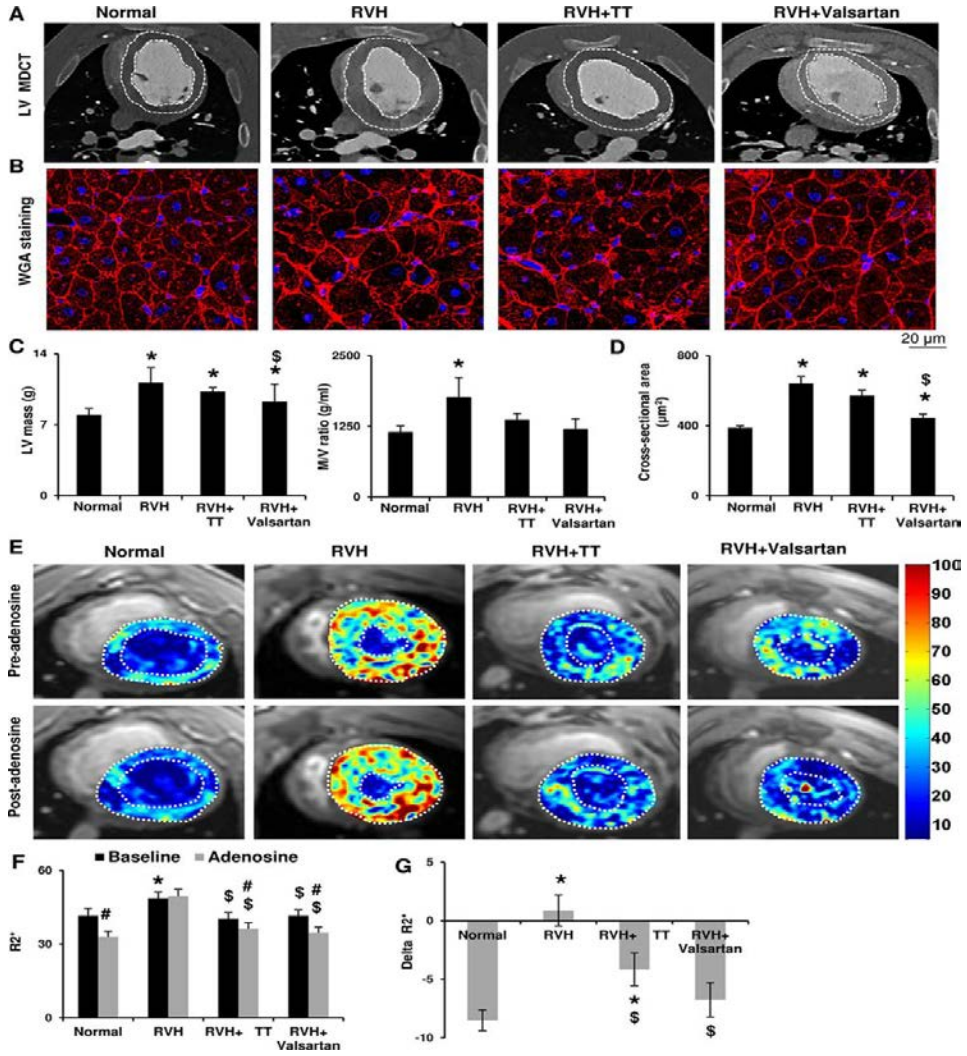
Role of nuclear unphosphorylated STAT3 in angiotensin II type 1 receptor-induced cardiac hypertrophy





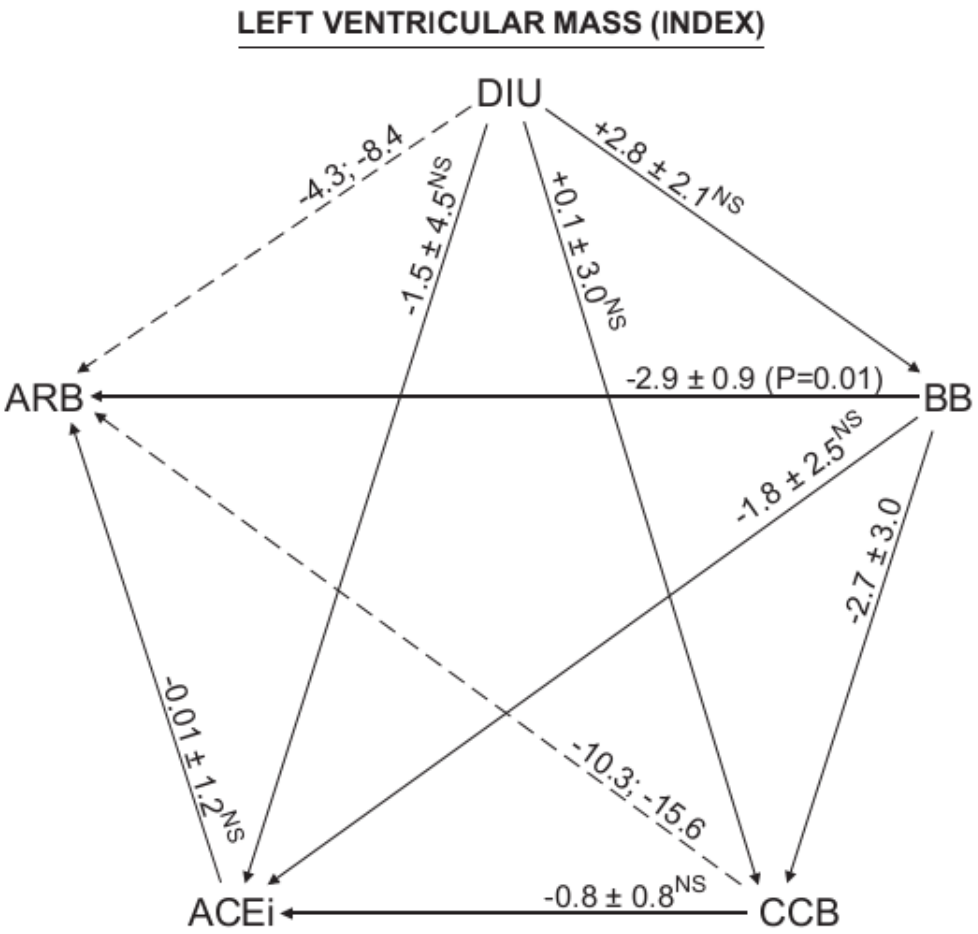
Yue, Cardiovascular Res Ad , 2009

Left ventricular (LV) structure in normal, renovascular hypertension (RVH)



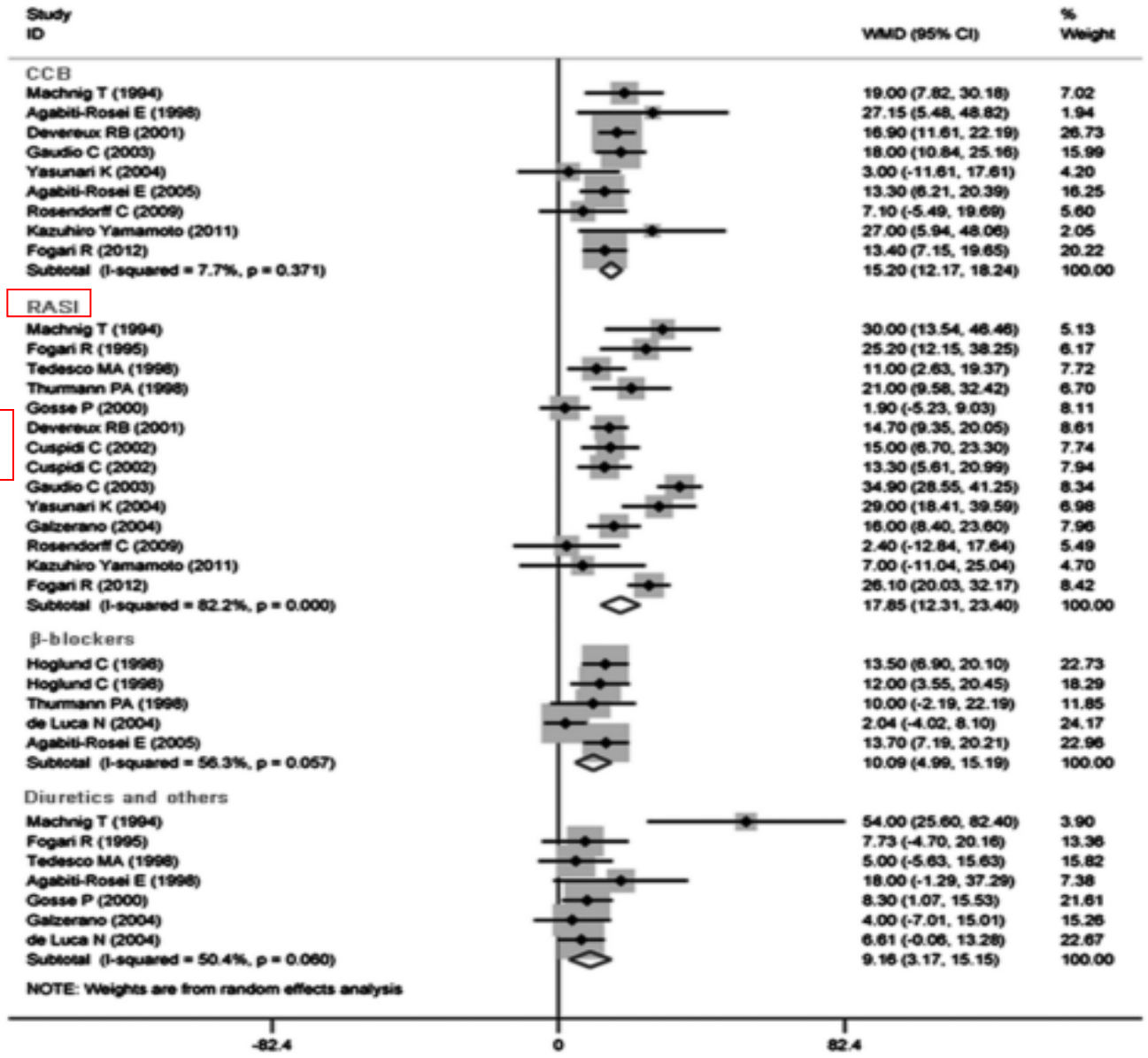
Zhang, Hypertension, 2014

RAS inhibitors and LVM



Fagard, Hypertension 2009

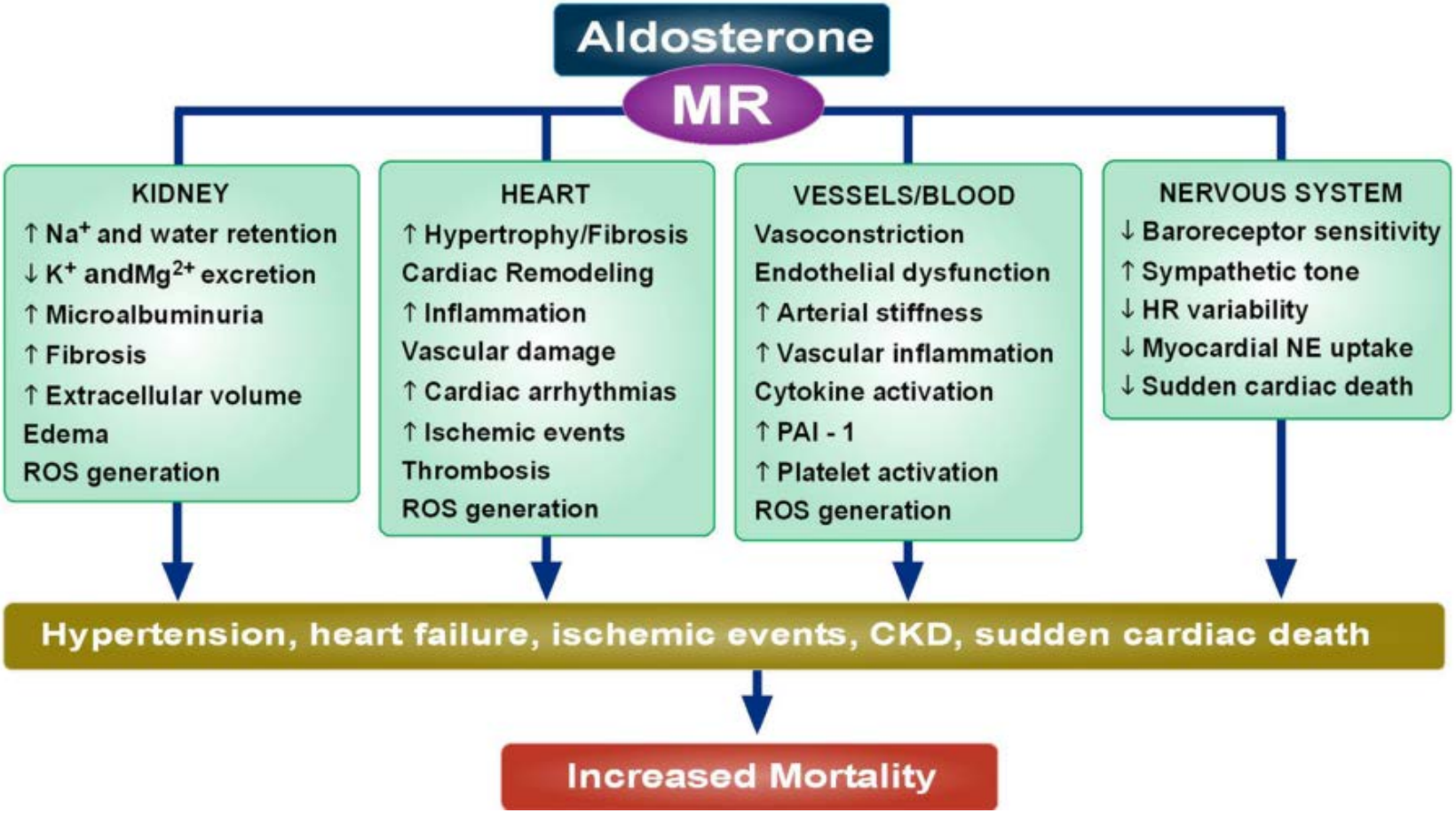
LVH and RAS inhibitors



-17.85 g m^{-2}

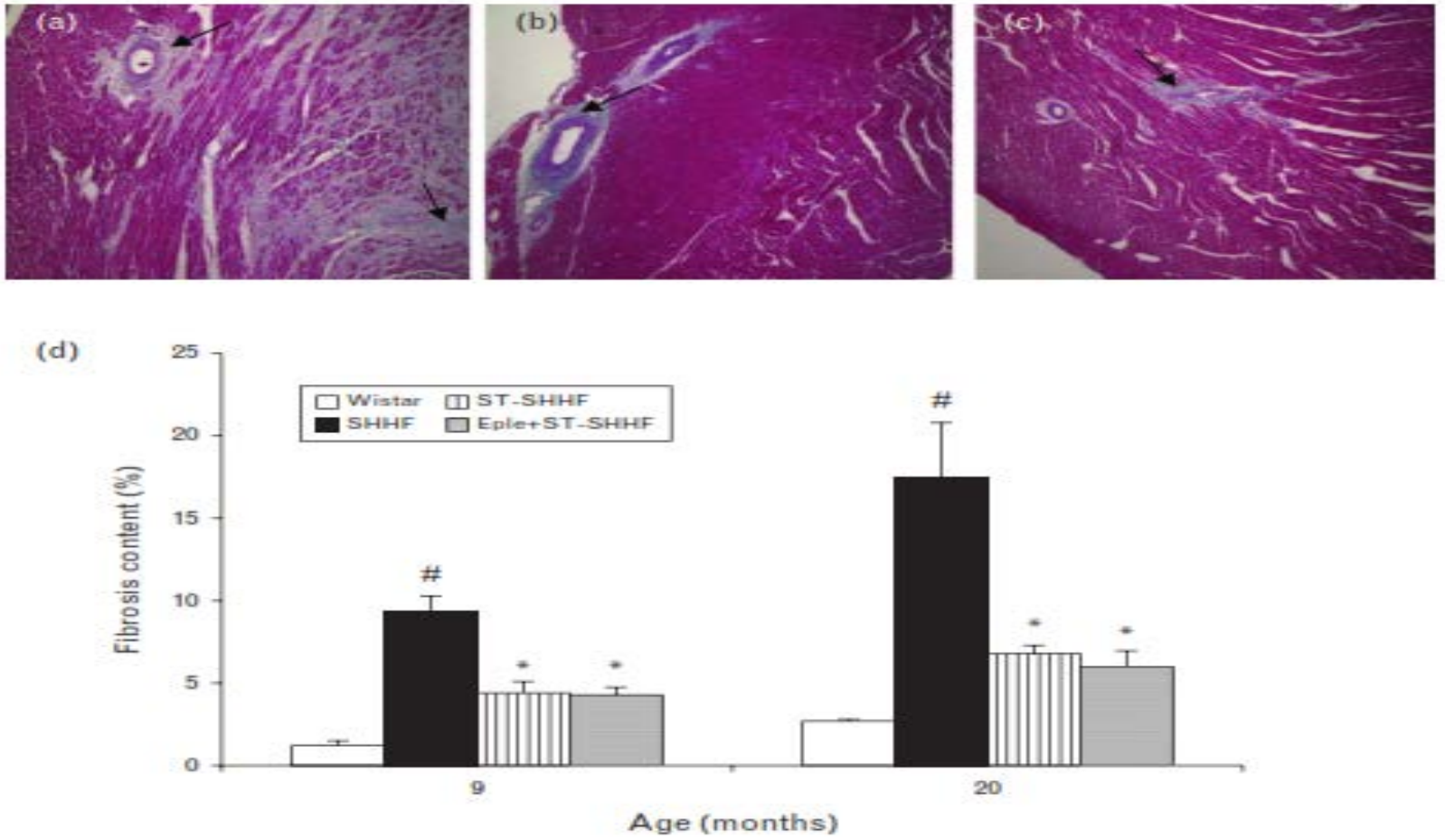
Zang, J H Hyperten 2013

Aldosterone and Heart



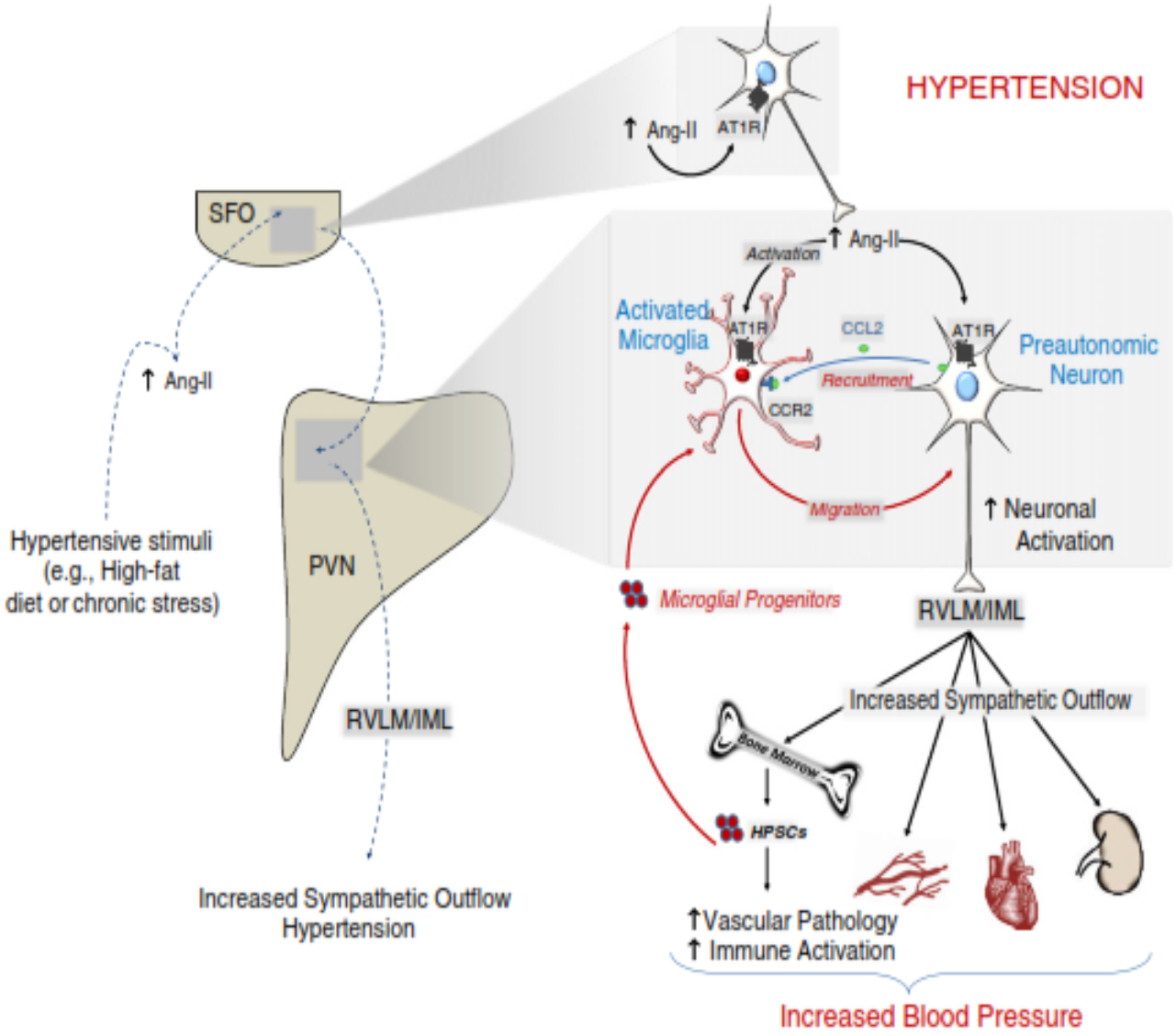
Tamargo, Sem Nephrol 2014

Eplerenone enhances cardioprotective effects of standard heart failure therapy through matricellular proteins in hypertensive heart failure



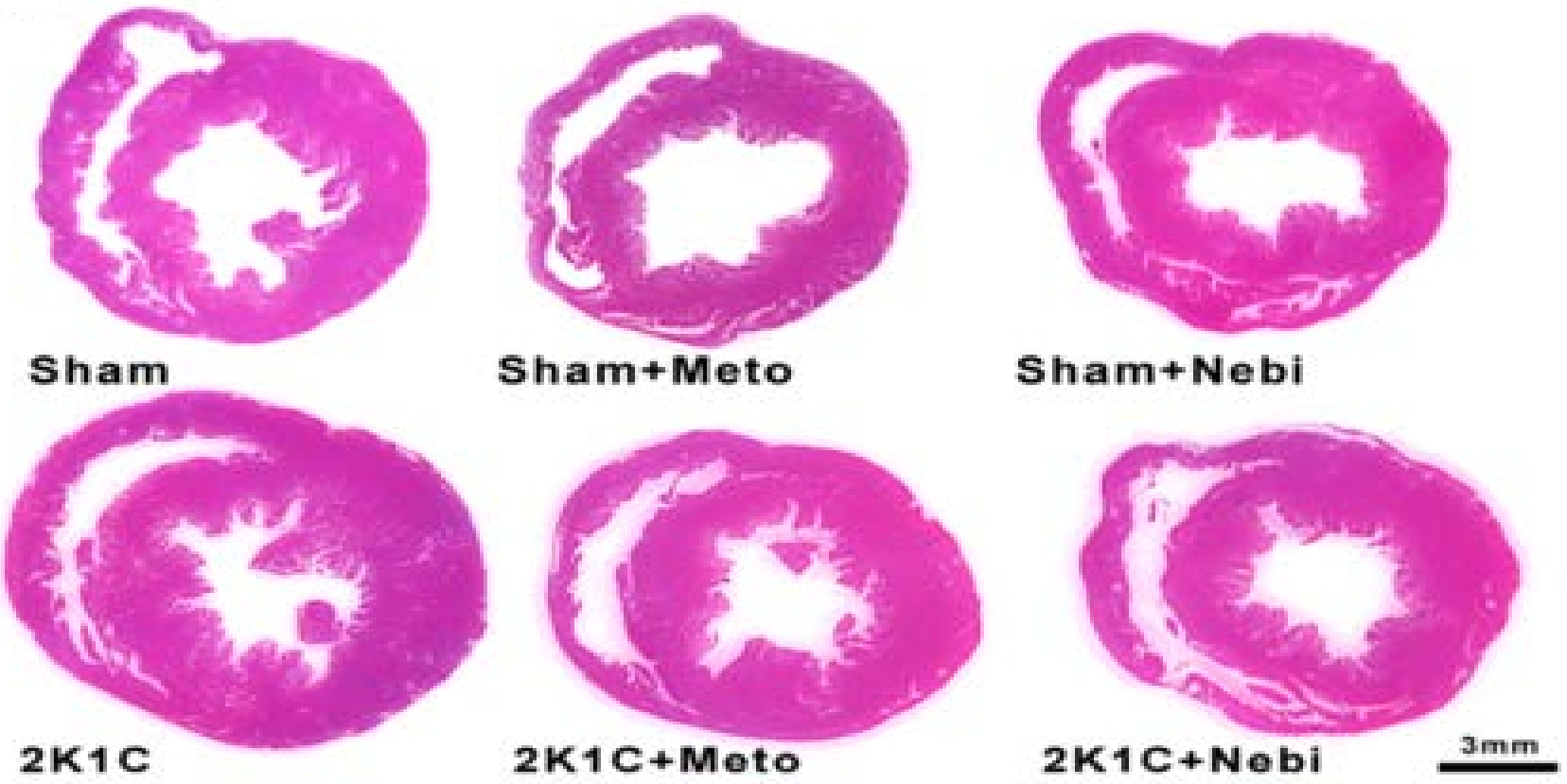
Munoz-Pacheco, J Hypertension 2013

SNC and LVM



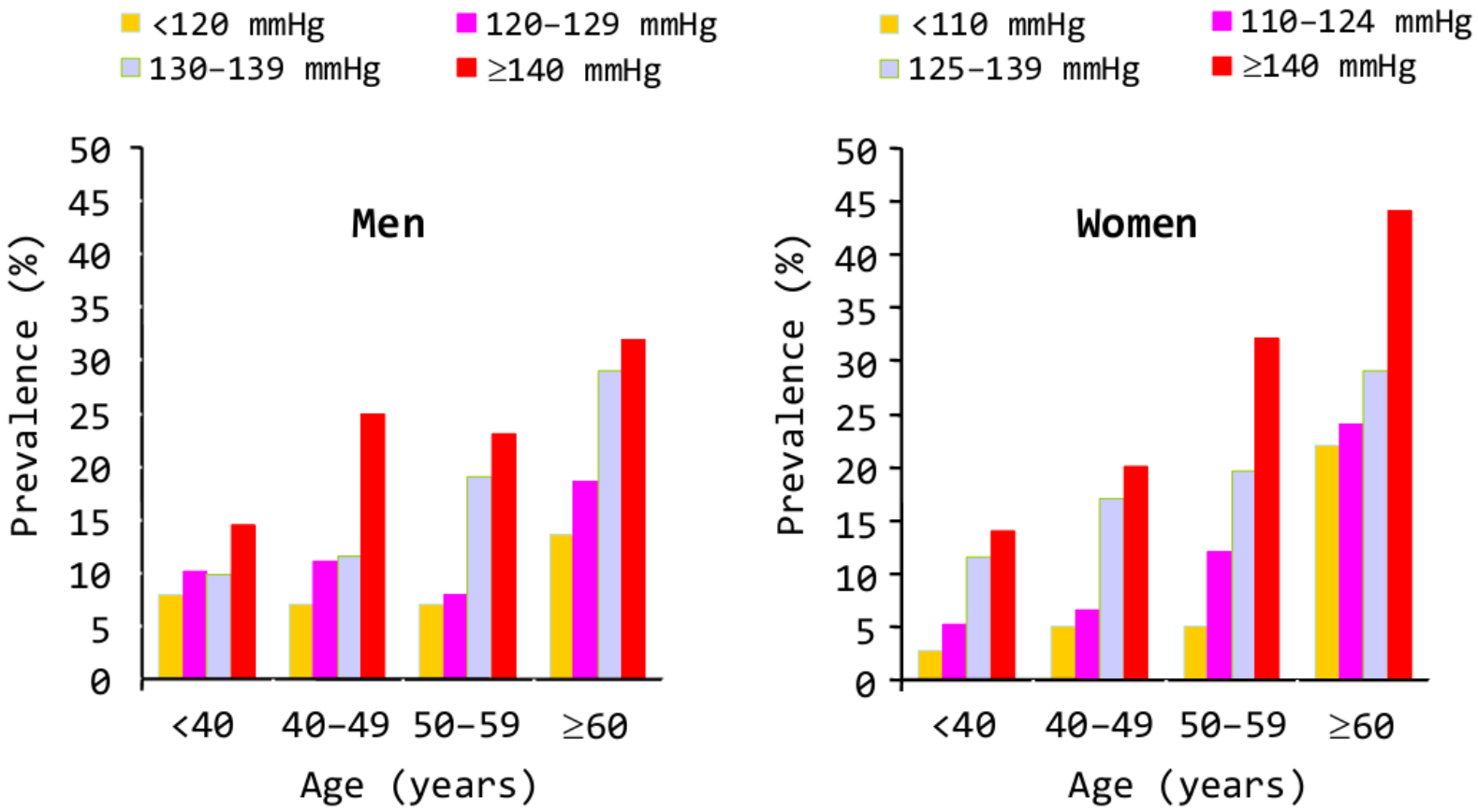
de Kloet, Pharmacology & Therapeutics, 2013

ß1-Adrenergic blockers exert antioxidant effects, reduce matrix metalloproteinase activity, and LVH



Rizzi, Free Rad Biol Med, 2014

Hypertension is a major risk factor for LVH



Levy et al. Ann Intern Med 1988;108:7–13

Prevalence of LVH

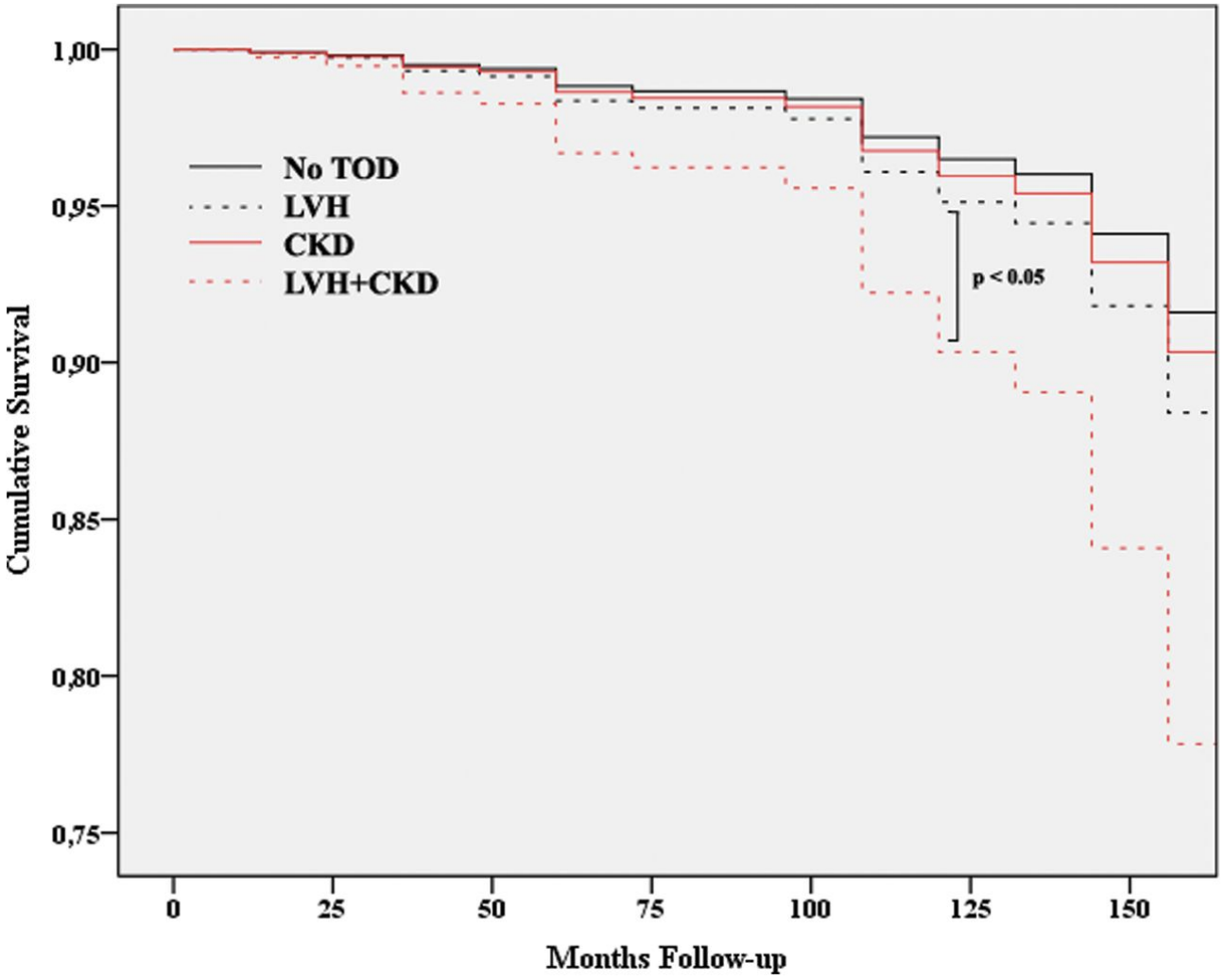
Author	ECG LVH criteria	ECHO LVH criteria	Prevalence of LVH (%)	
			ECG	ECHO
Verdecchia [13]	Wilson	LVMI >125 g/m^2	0.6	27.2
	LV strain	LVMI >51 gm$^{2.7}$	3.0	49.9
	Romhilt-Estes		4.8	
	Gubner Ungerleider		7.1	
	Sokolow -Lyon		11.1	
	Cornell voltage		11.9	
	Perugia score		18.4	
Salles [17]	Sokolow -Lyon, or Cornell voltage	LVM >294 g (M); >198 g (F)	18.9	50.0
Verdecchia [18]	Perugia score	LVMI >49.2 gm$^{2.7}$ (M); >46.7 gm$^{2.7}$ (F)	17.1	47.8
Martinez [19]	Cornell voltage	LVMI >134 gm^2 (M); >110 gm^2 (F)	9.0	32.0
Schneider [21]	Cornell voltage	LVMI >134 gm^2 (M); >110 gm^2 (F)	5.0	37.0
	Cornell voltage-duration product		9.5	
Cuspidi [29]	Sokolow–Lyon	LVMI >125 gm^2 (M); >110 gm^2 (F)	10.4	36.5
Radulescu [32]	Sokolow–Lyon or Cornell voltage-duration product	LVMI >125 g/m^2	40.0	41.4
Salles [38]	Sokolow–Lyon	LVMI >125 gm^2 (M)	20.5	75.7
	Cornell voltage	>110 gm^2 i(F)	21.9	
	Cornell voltage-duration product		25.4	

F, females; LVH, left ventricular hypertrophy; LVMI, left ventricular mass index; M, males.

EKG: 18 % ECHO 32%

Cuspidi et al J of Hypertens ott 2012

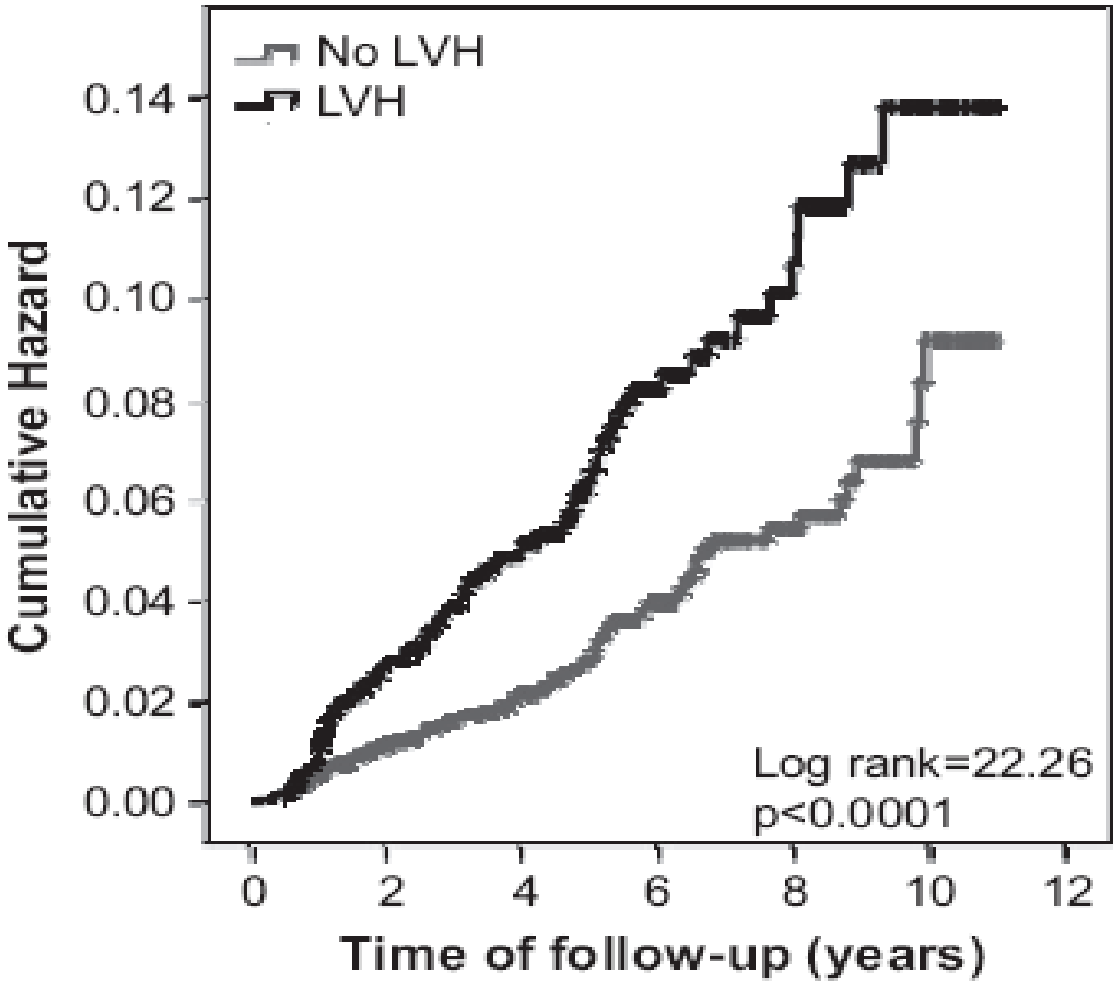
Cox multivariable free-time events curves in relation to target-organ damage (TOD) groups.



Carpinella, Am J Hypertens 2014

Prediction risk of LVH

Pts=5380



De Simone, Hypertension 2010

Risk Reduction After Regression of Echocardiographic Left Ventricular Hypertrophy

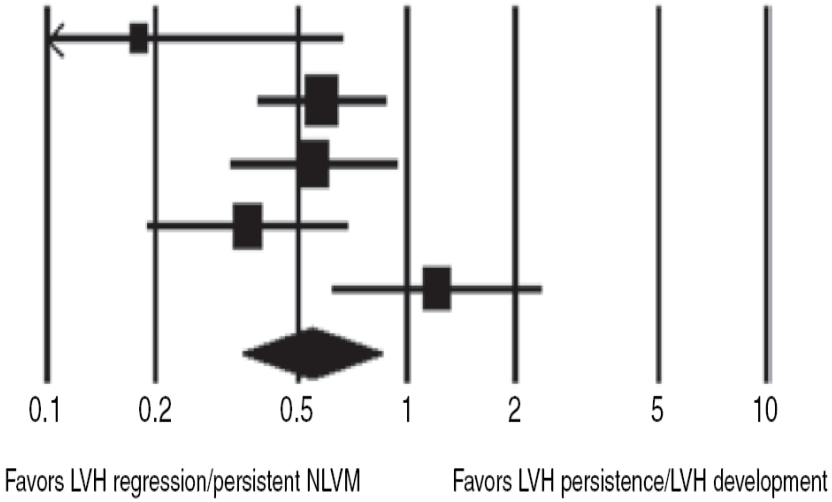
(3,149 patients)

Total cardiovascular events

Study name	Hazard ratio	Lower limit	Upper limit	*Z* value	*P* value
Verdecchia 1998	0.180	0.049	0.664	–2.575	0.010
Devereux 2004	0.580	0.386	0.873	–2.614	0.009
Muiesan 2007	0.550	0.322	0.938	–2.195	0.028
Pierdomenico 2008	0.360	0.190	0.681	–3.141	0.002
Yasuno 2009	1.210	0.620	2.361	0.559	0.576
	0.542	0.348	0.844	–2.710	0.007

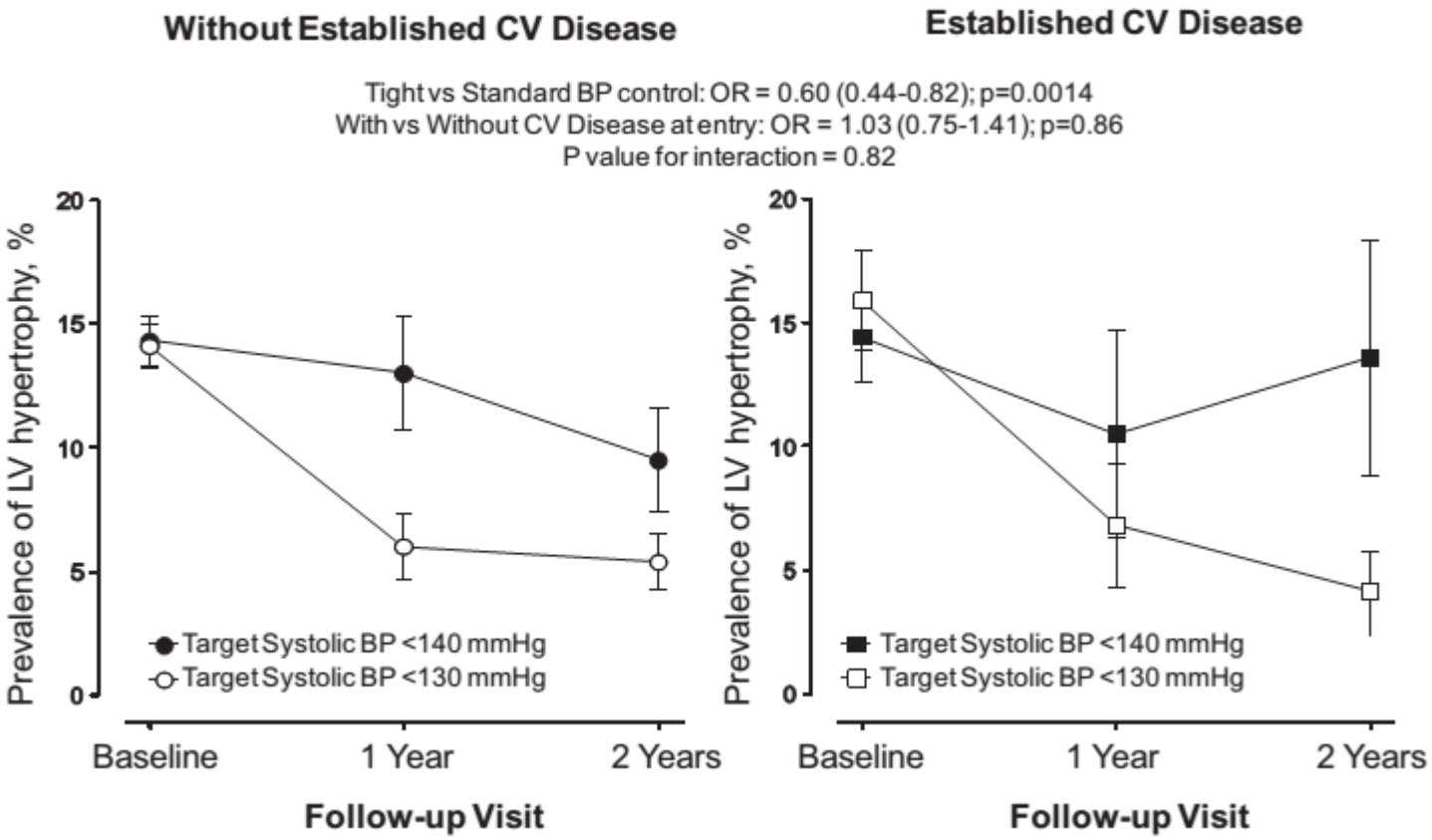
Statistics for each study

Hazard ratio and 95% CI



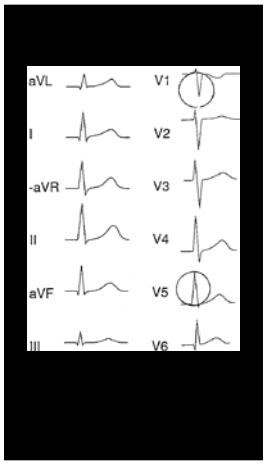
Pierdomenico, Am J Hyperten 2010

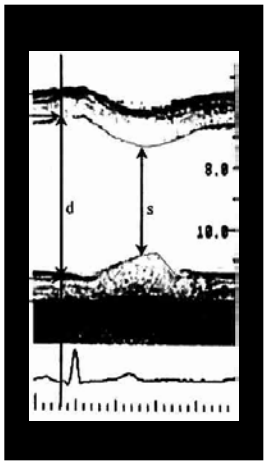
BP target and LVH

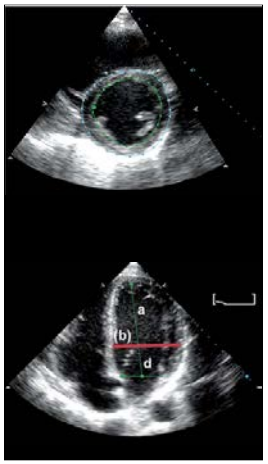


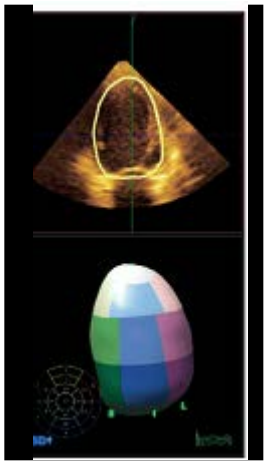
Reboldi Hypertension 2014

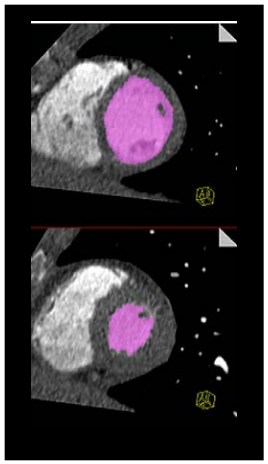
Methods of assessing hypertensive cardiomiopathy











	ECG	M-mode echocardiography	2D echocardiography	3D echocardiography	Cardiac MRI
Sensitivity	Low	Moderate	High	High	High
Specificity	High	High	High	High	High
Cost	Low	Moderate	Moderate	Moderate	High
Availability	High	High	High	Low	Low
Complexity	Low	Low	Moderate	High	Moderate
Interpatient reproducibility	Moderate	Moderate	Moderate	Low	High

Ruilope Am J Hypert 2008

Search for asymptomatic organ damage, cardiovascular disease

Recommendations	Class[a]	Level[b]	Ref.[c]
Heart			
An ECG is recommended in all hypertensive patients to detect LVH, left atrial dilatation, arrhythmias, or concomitant heart disease.	I	B	149, 150, 151, 154
In all patients with a history or physical examination suggestive of major arrhythmias, long-term ECG monitoring, and, in case of suspected exercise-induced arrhythmias, a stress ECG test should be considered.	IIa	C	-
An echocardiogram should be considered to refine CV risk, and confirm ECG diagnosis of LVH, left atrial dilatation or suspected concomitant heart disease, when these are suspected.	IIa	B	156, 158, 160, 163, 164
Whenever history suggests myocardial ischaemia, a stress ECG test is recommended, and, if positive or ambiguous, an imaging stress test (stress echocardiography, stress cardiac magnetic resonance or nuclear scintigraphy) is recommended.	I	C	-

Mancia et al. ESH/ESC 2013

Cut-off values for parameters of LV remodelling and diastolic function in hypertension

Parameter	Abnormal if
LV mass index (g/m²)	>95 (women) >115 (men)
Relative wall thickness (RWT)	>0.42
Diastolic function: Septal e' velocity (cm/sec) Lateral e' velocity (cm/sec) LA volume index (mL/m²)	 <8 <10 ≥34
LV Filling pressures : E/e' (averaged) ratio	 ≥13

LA, left atrium; LV, left ventricle; RWT, relative wall thickness.

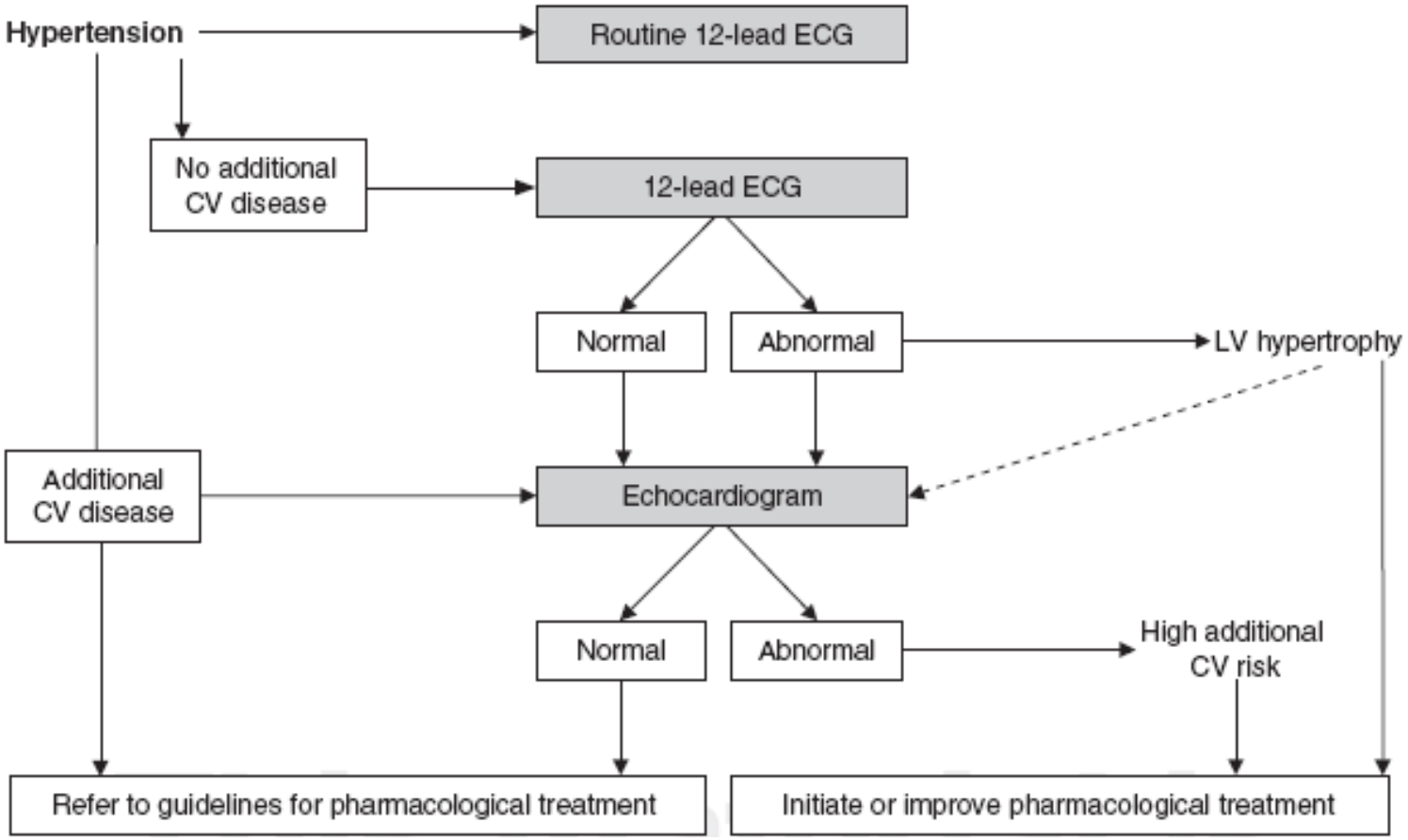
Mancia et al. ESH/ESC 2013

Markers of LVM regression

Marker of organ damage	Sensitivity for changes	Time to change	Prognostic value of changes
LVH/ECG	Low	Moderate (>6 months)	Yes
LVH/echo	Moderate	Moderate (>6 months)	Yes
LVH/cardiac magnetic resonance	High	Moderate (>6 months)	No data

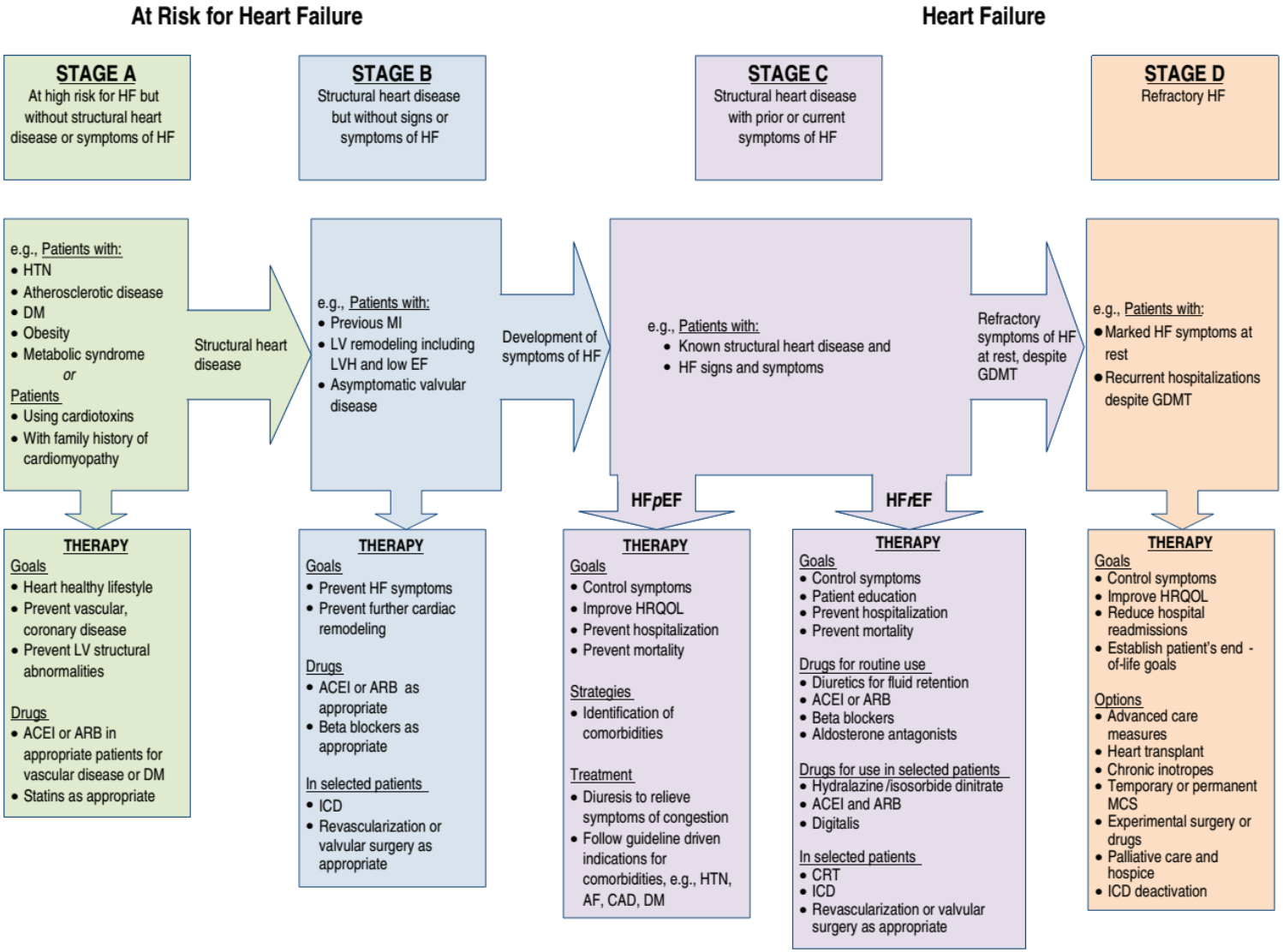
ESH/ESC 2013 Guidelines

WORK-UP HYPERTENSIVE CARDIOPATHY



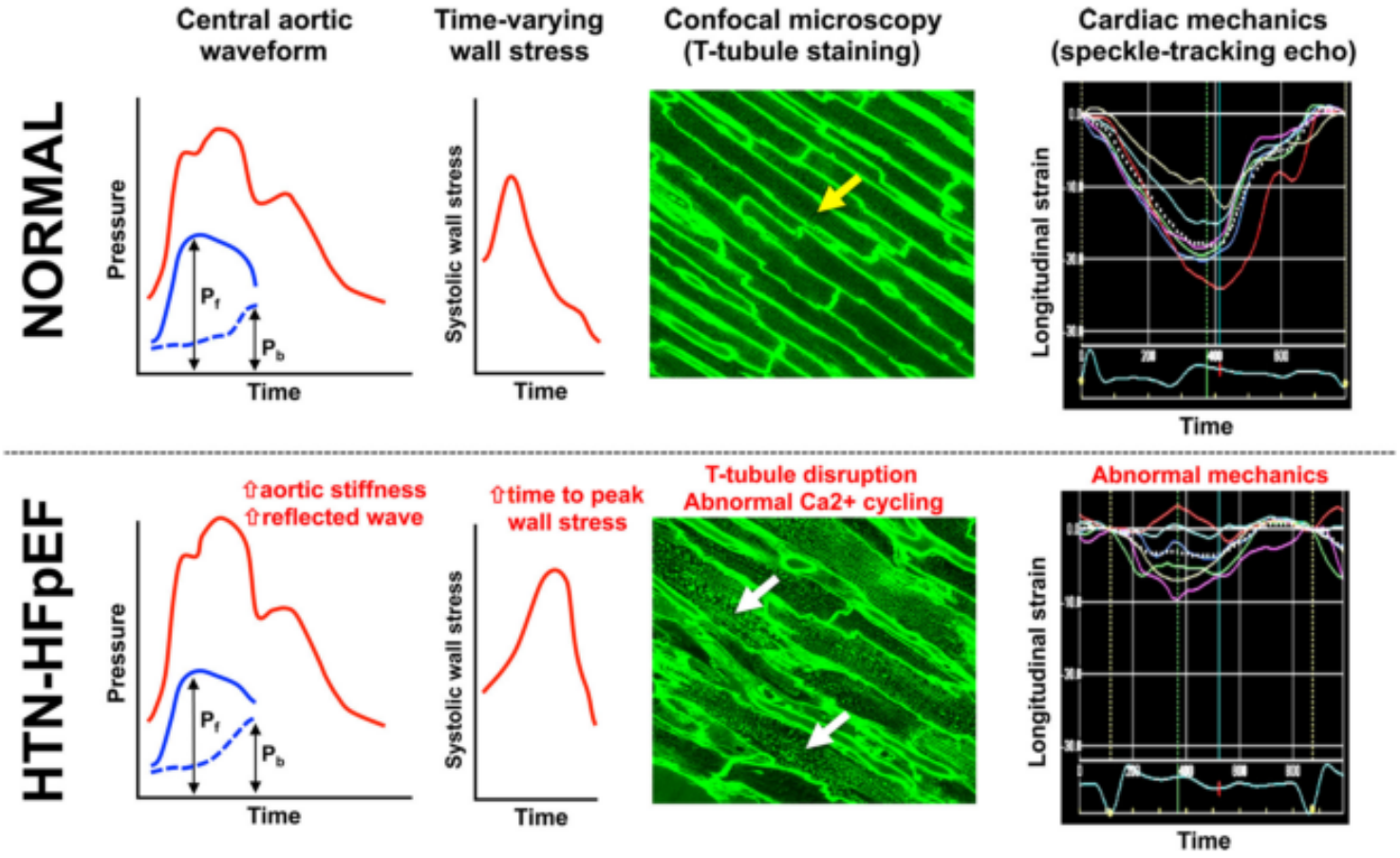
SIIA,SIC,Ital Heart J . 2008

Staging Heart disease



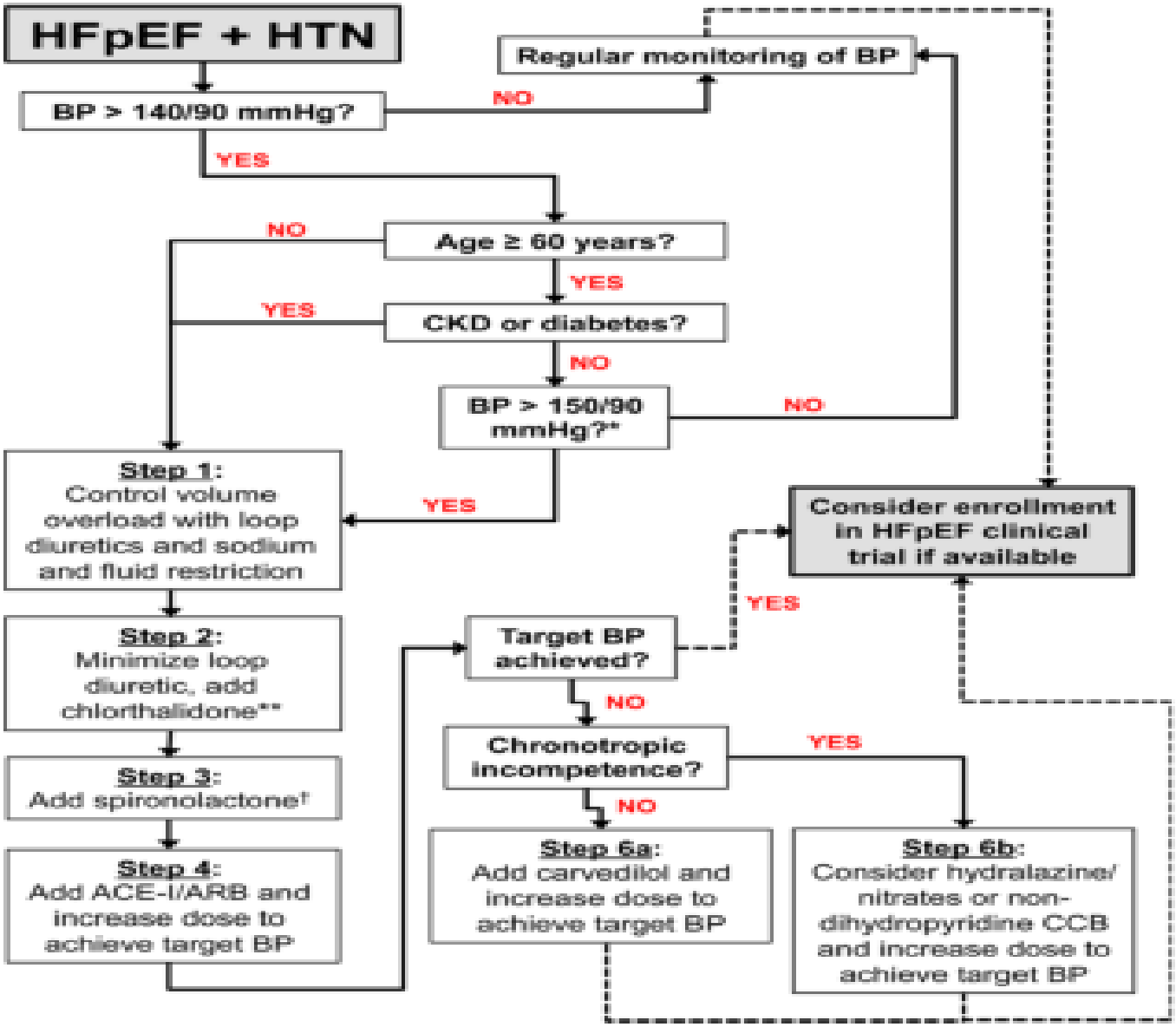
Yancy Circulation 2013 HF Guidelines

Pathophysiologic schema of hypertension-induced HFpEF



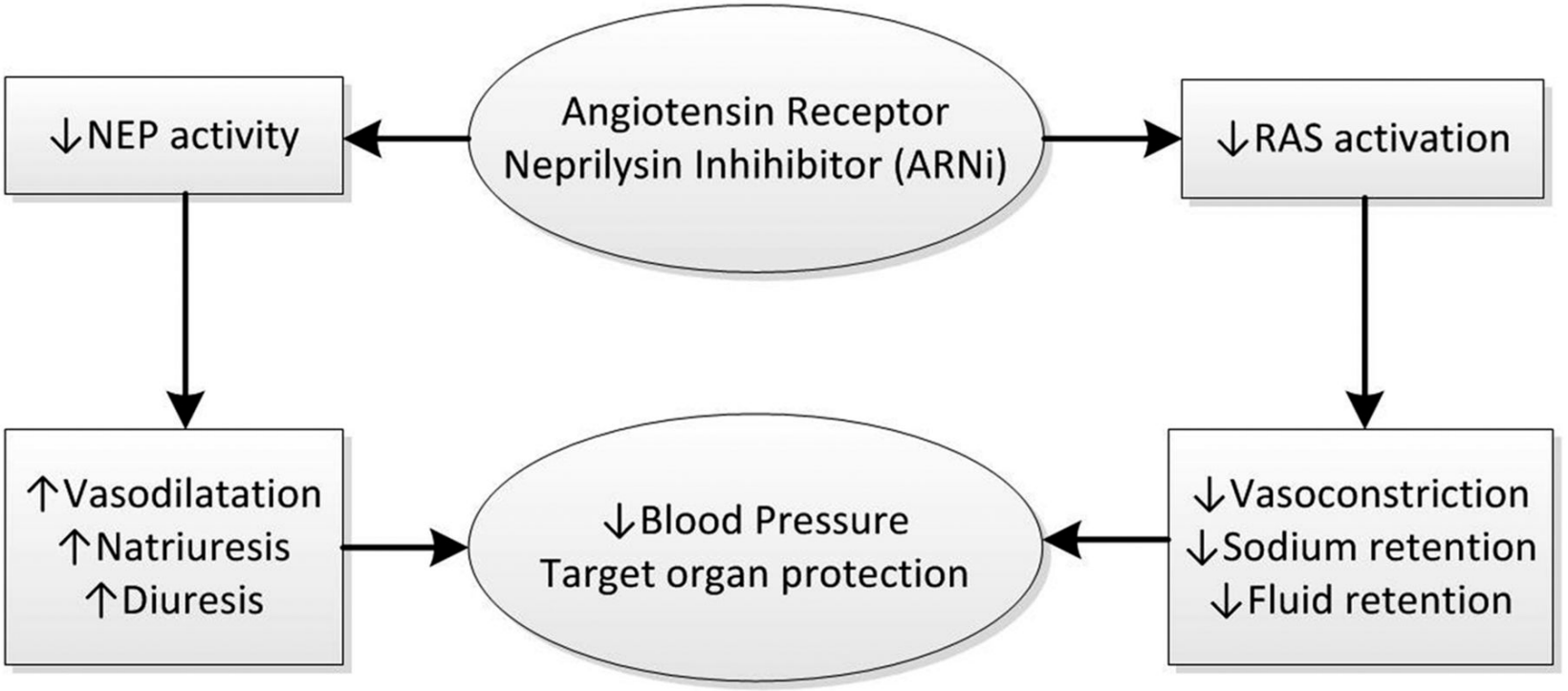
Oktay, Curr Cardiol Rep 2014

Hypertension treatment algorithm for patients with heart failure and preserved ejection fraction (HFpEF)

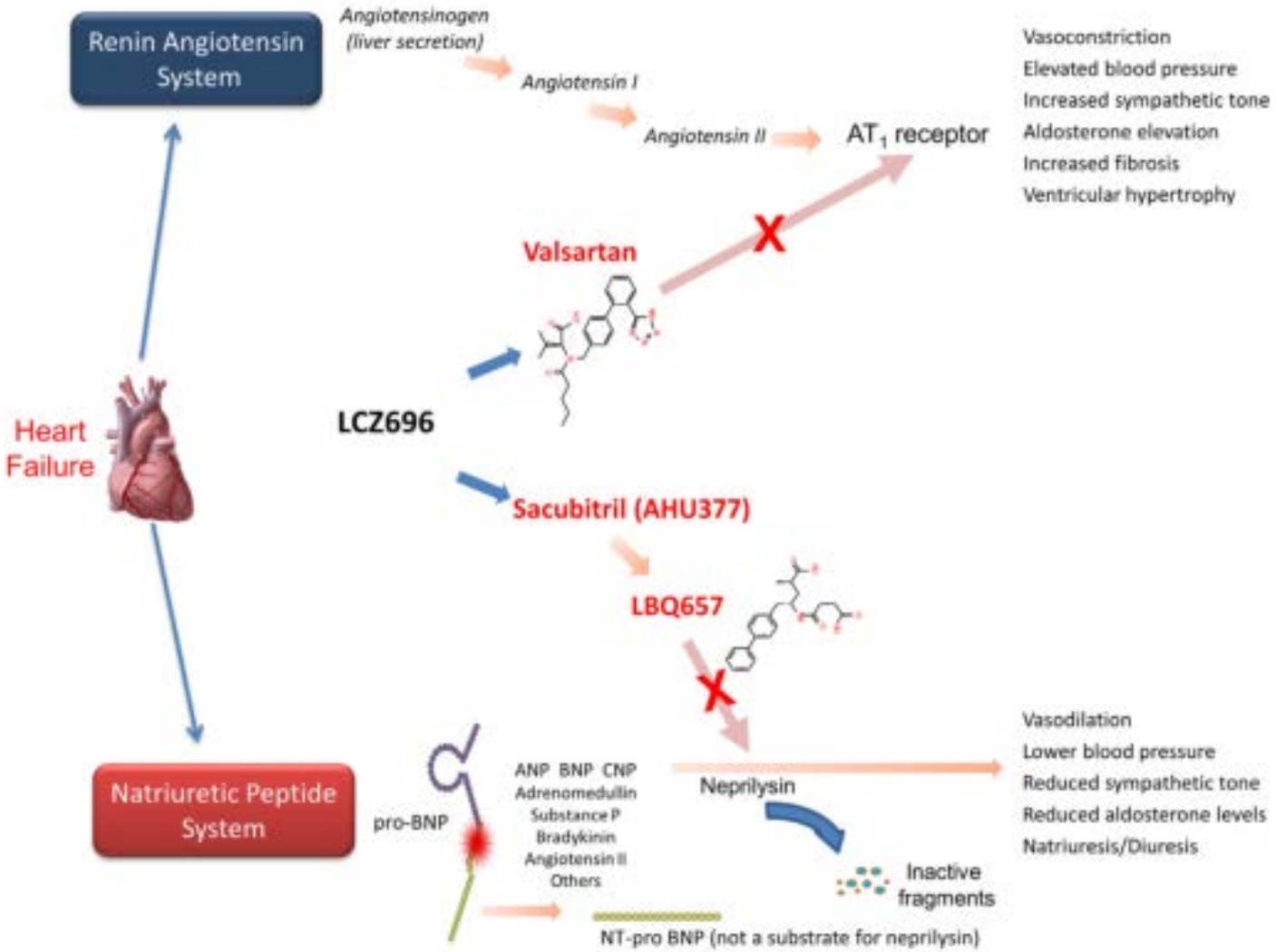


Oktay, Curr Cardiol Rep 2014

Mechanism of action of ARNi

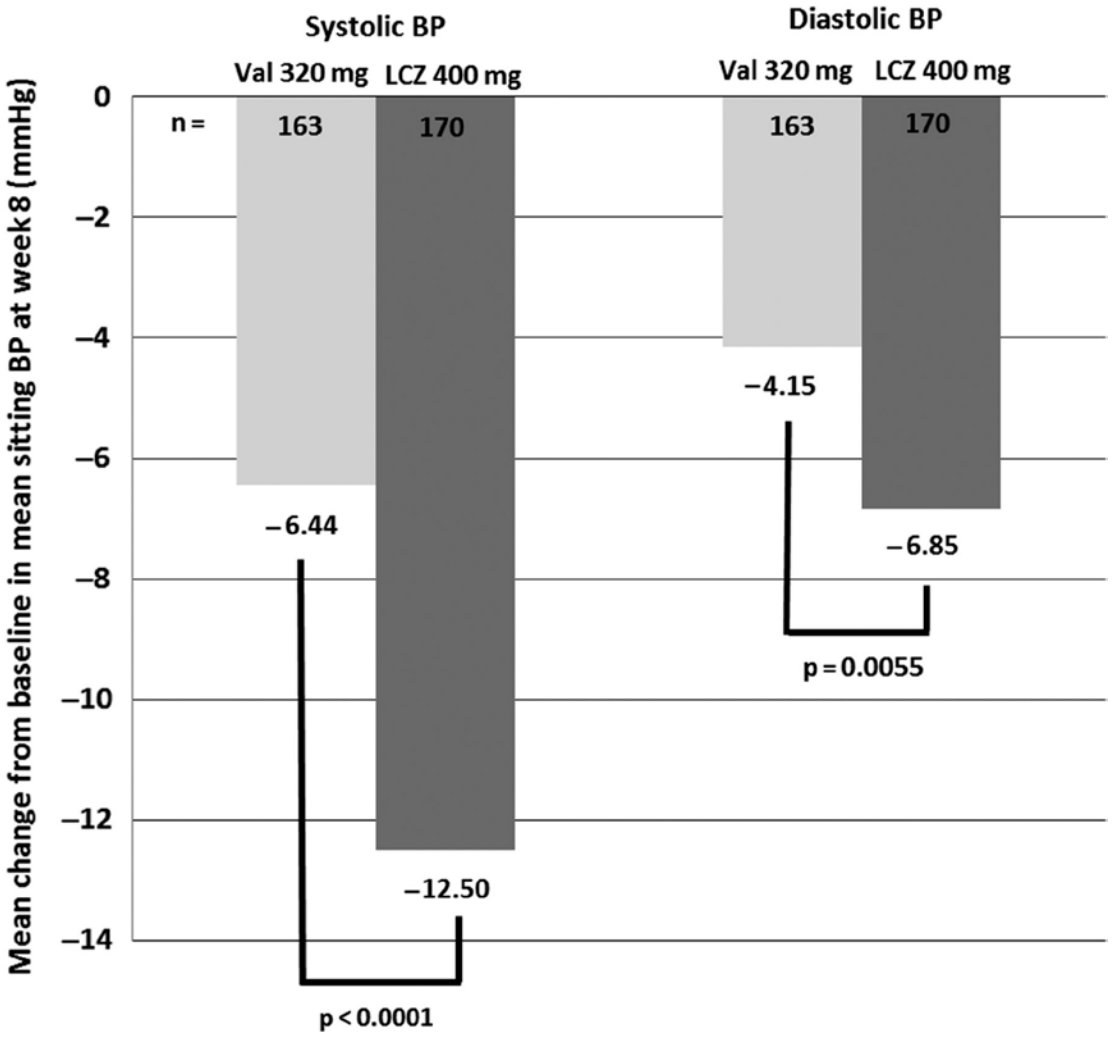


Judge P et al. Nephrol. Dial. Transplant. 2014



Vardeny,JACC, 2014

Difference in mean sitting SBP and DBP at week 8 (mmHg)



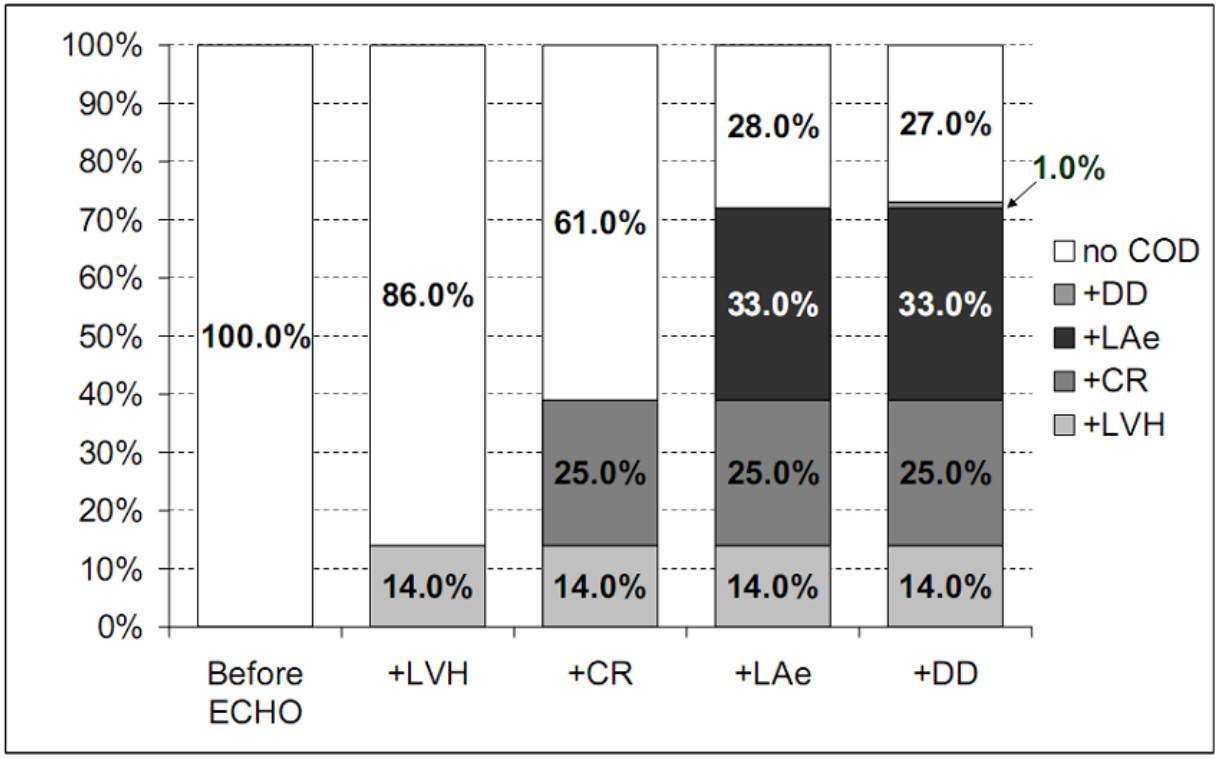
Judge P et al. Nephrol. Dial. Transplant. 2014

TABLE 1 Clinical Trials of LCZ696

First Author (Study) (Ref. #)	Sample Size and Patient Population	Study Medications	Study Design	Main Findings
Ruilope et al. (19)	n = 1,328 with hypertension	LCZ696 100, 200, and 400 mg vs. valsartan 80, 160, and 320 mg vs. AHU377 200 mg	Randomized controlled dose-ranging study; primary end point was reduction in BP between groups at 8 weeks	Significant reductions in systolic and diastolic BPs with LCZ696 200 mg vs. valsartan 160 mg and with LCZ696 400 mg vs. valsartan 320 mg; significant reduction in ambulatory BP with LCZ vs. valsartan
Kario et al. (20)	n = 309 Asians with hypertension	LCZ696 100, 200, and 400 mg vs. placebo	Randomized controlled dose-ranging study	Significant reductions in systolic and diastolic BPs, pulse pressure, and ambulatory pressure with LCZ696
Solomon et al. (PARAMOUNT) (22)	n = 301 with HFpEF	LCZ696 200 mg bid vs. valsartan 160 mg bid	Randomized controlled trial; primary end point was reduction in NT-proBNP at 12 weeks	Significant reduction in NT-proBNP at 12 wk with LCZ696, as well as left atrial volume at 36 wk; improvement in NYHA class in patients receiving LCZ696 vs. placebo
McMurray et al. (PARADIGM-HF) (26)	n = 8,442 with HFrEF	LCZ696 200 mg bid vs. enalapril 10 mg bid	Randomized controlled trial; primary outcome was cardiovascular death or HF hospitalization	Significant reductions in the primary outcome (20%), cardiovascular death (20%), and all-cause mortality (16%) with LCZ696 vs. enalapril

Vardeny,JACC, 2014

Ecocardiographic abnormalities & Hypertension

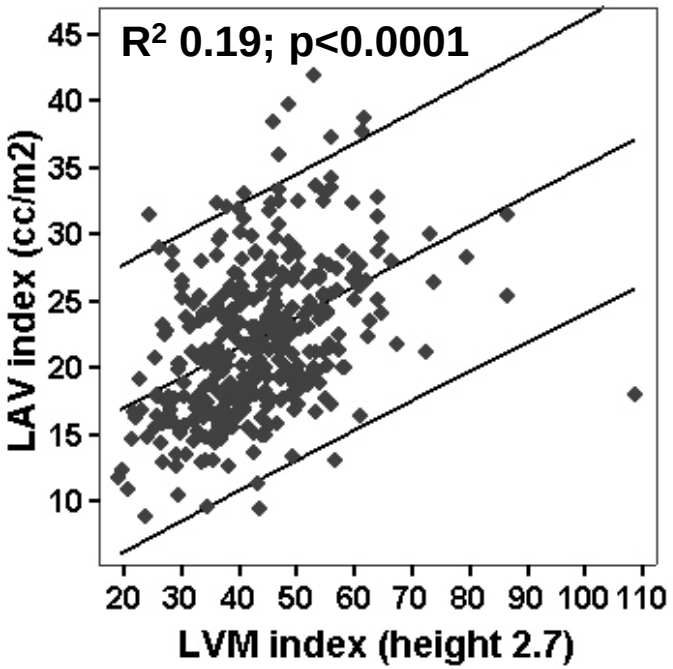


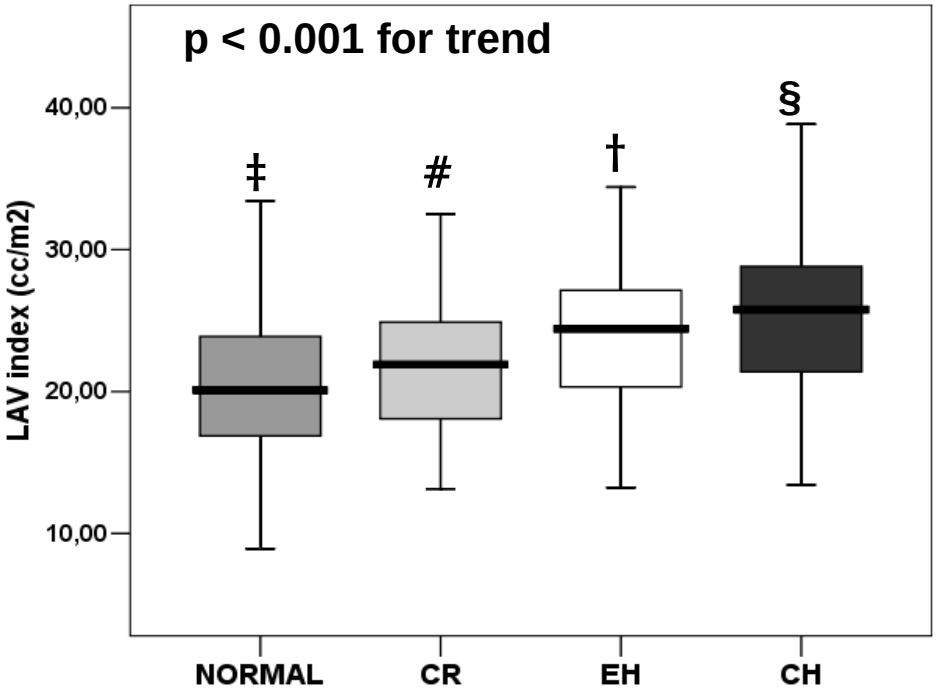
Milan, J Human Hypert 2010

Left atrium

394 pazienti

LAV index = 12.4+ 0.23*LVMi$^{2.7}$





‡ p<0.0001 vs. CH and EH

p 0.0004 vs CH and p=0.01 vs. EH

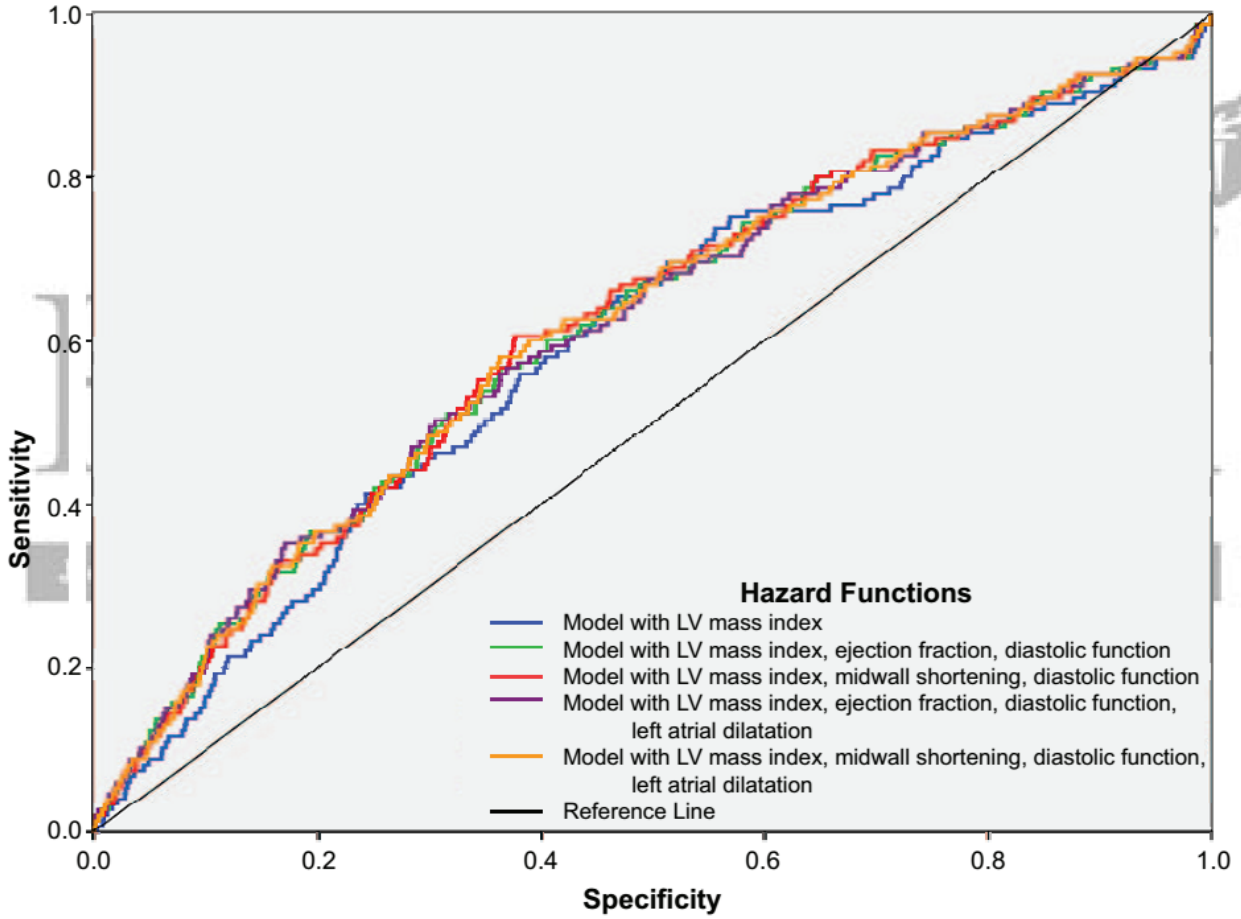
† p<0.0001 vs Normal and p=0.01 vs. CR

§ p<0.0001 vs Normal and p=0.0004 vs. CR

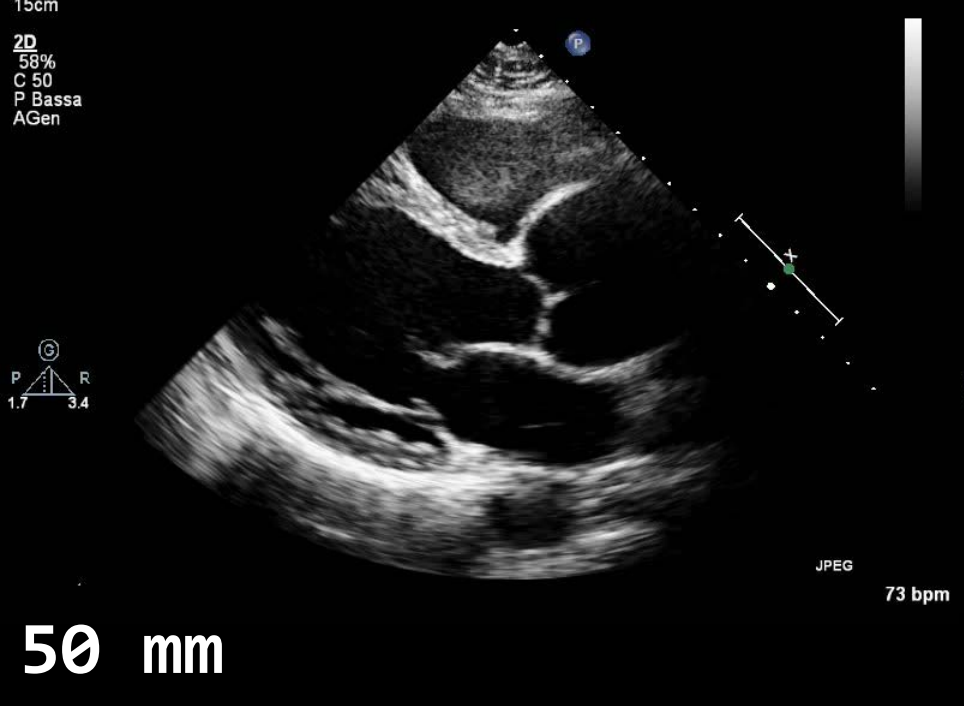
Milan, Journal of Human Hypertension 2009

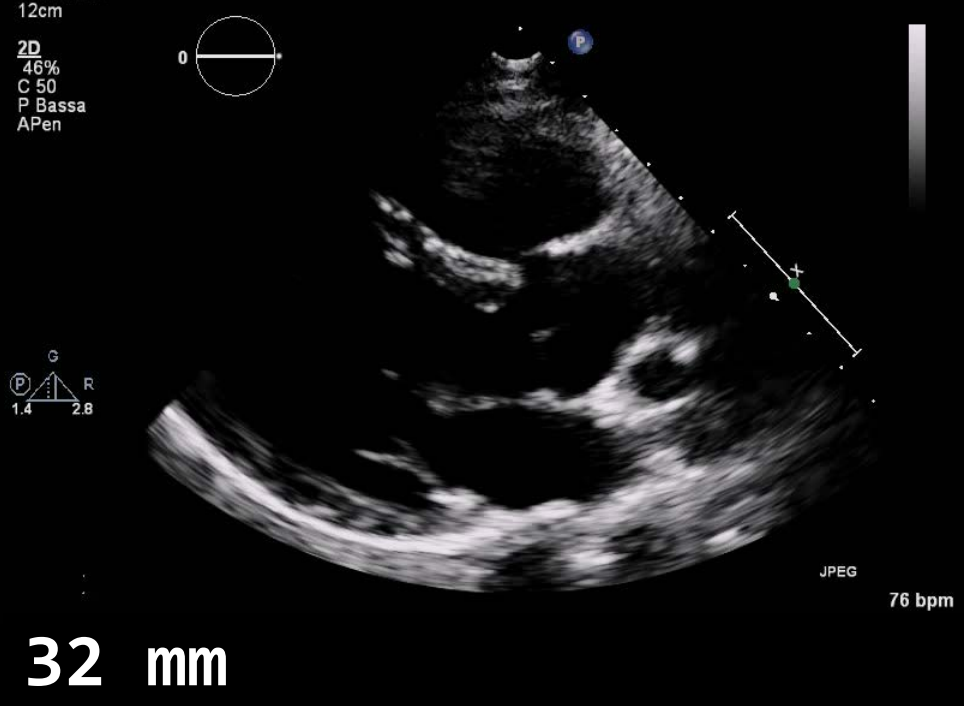
Does Information on Systolic and Diastolic Function Improve Prediction of a Cardiovascular Event by Left Ventricular Hypertrophy in Arterial Hypertension?

Giovanni de Simone, Raffaele Izzo, Marcello Chinali, Marina De Marco, Giuseppina Casalnuovo, Francesco Rozza, Daniela Girfoglio, Gianni Luigi Iovino, Bruno Trimarco, Nicola De Luca



De Simone Hypertension 2010





Prevalence

9.1 %

12% males

4% females

Valsalva sinuses

Echocardiographic aortic root dilatation in hypertensive patients: a systematic review and meta-analysis

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J of Hypertens 2014

Aortic root

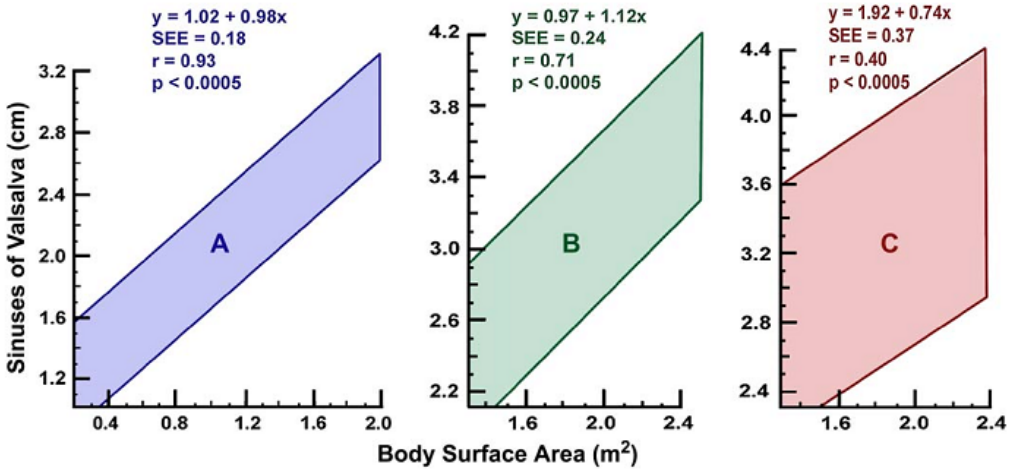


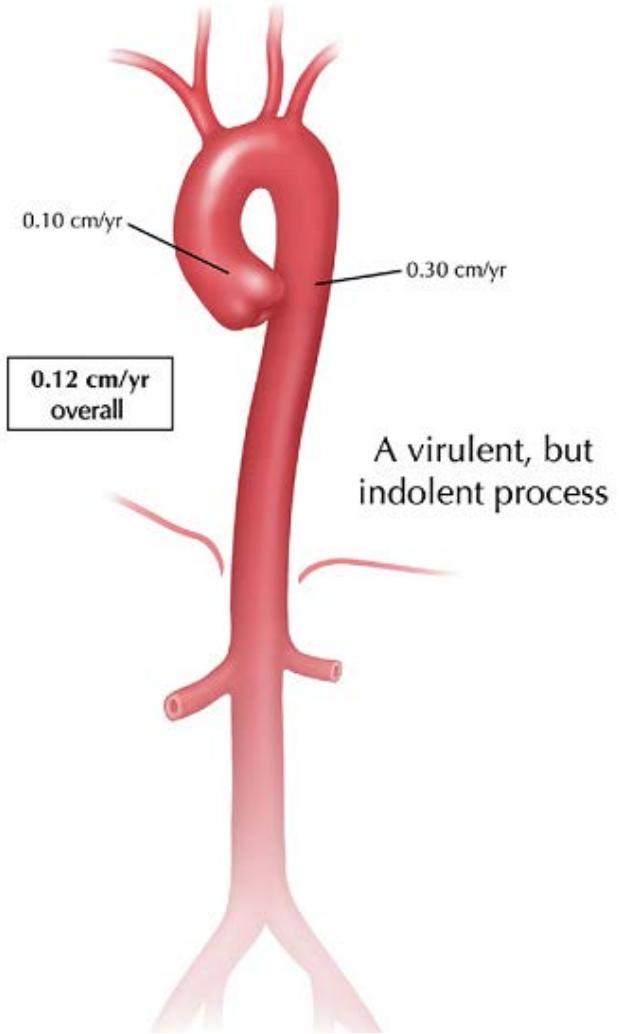
Figure 20 95% confidence intervals for aortic root diameter at the sinuses of Valsalva based on body surface area in: children and adolescents (A), adults aged 20–39 years (B), and adults aged 40 years or more (C).[132]

Roman et al Am H J 1989

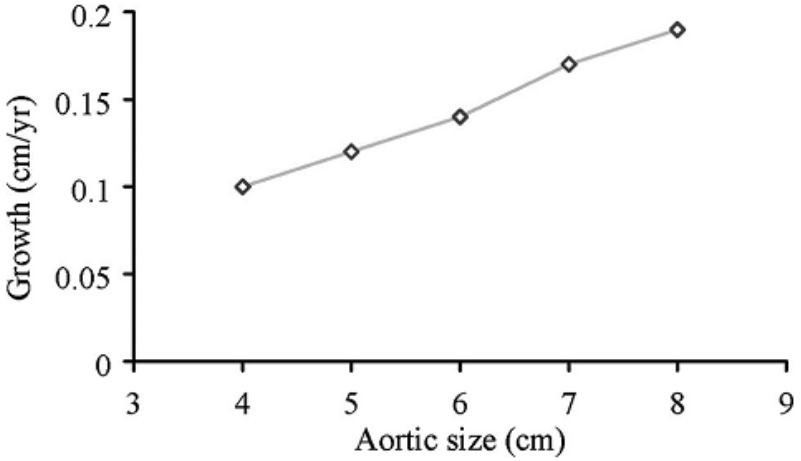
pBSA= 2.423+Age*0.009+BSA*0.461-0.267*Gender+0.261*1.96

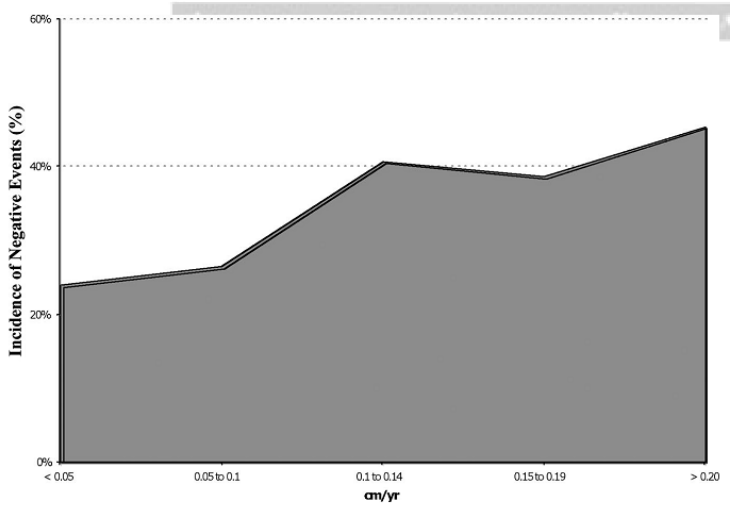
Devereux et al. Am J of Cardiol 2012

Increasing by age



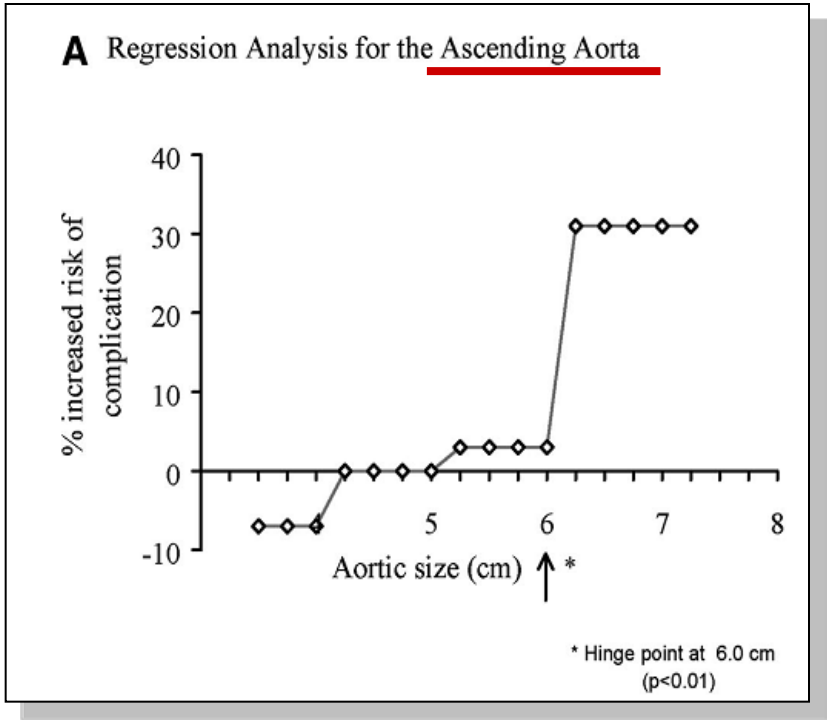
Elefteriades *JACC* 2010

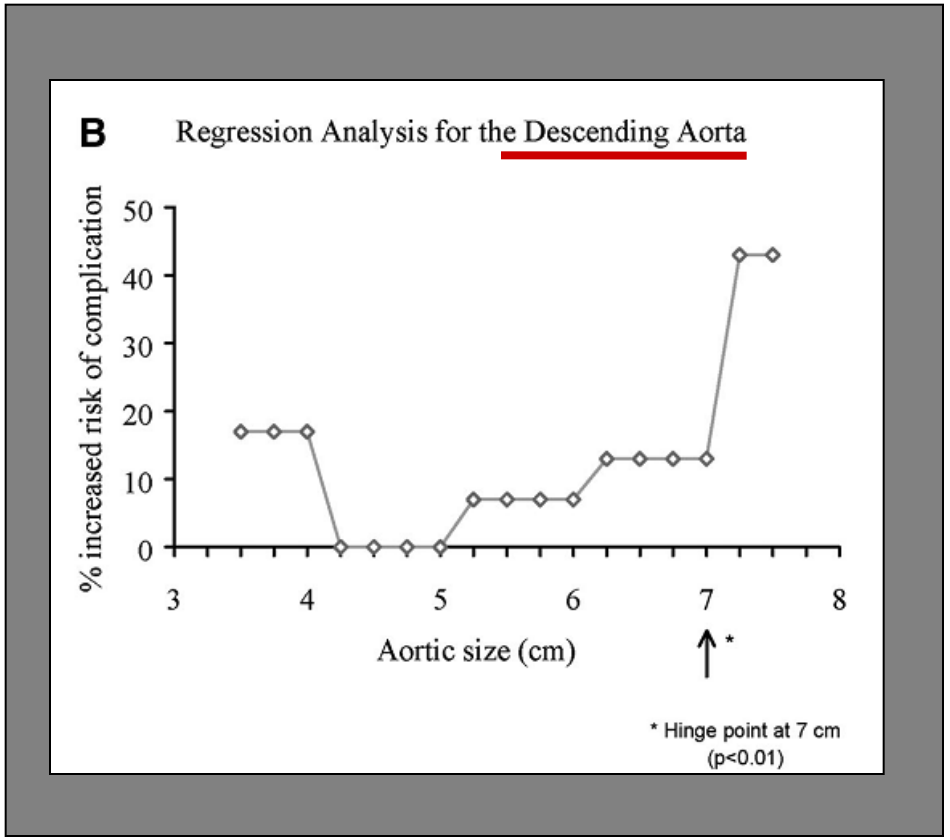




Coady et al. *Circulation* June 2010

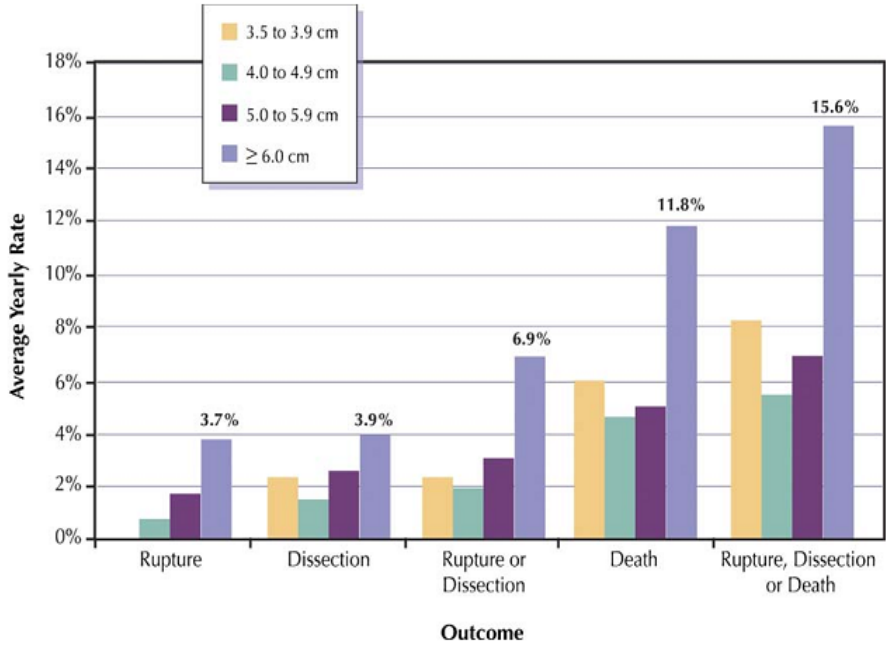
Risk of complications

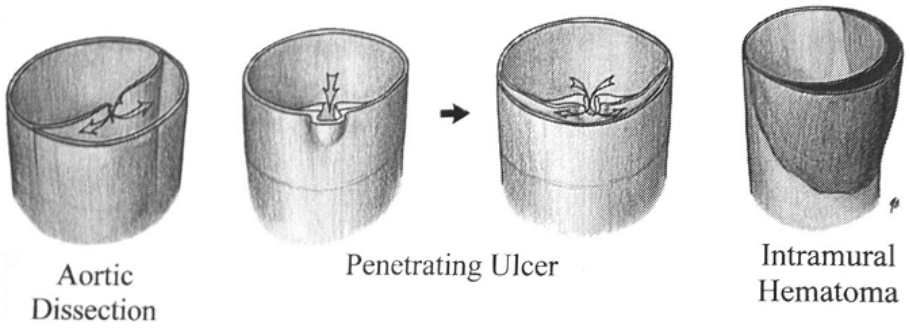




Coady et al. *Circulation* June 2010

Prognosis

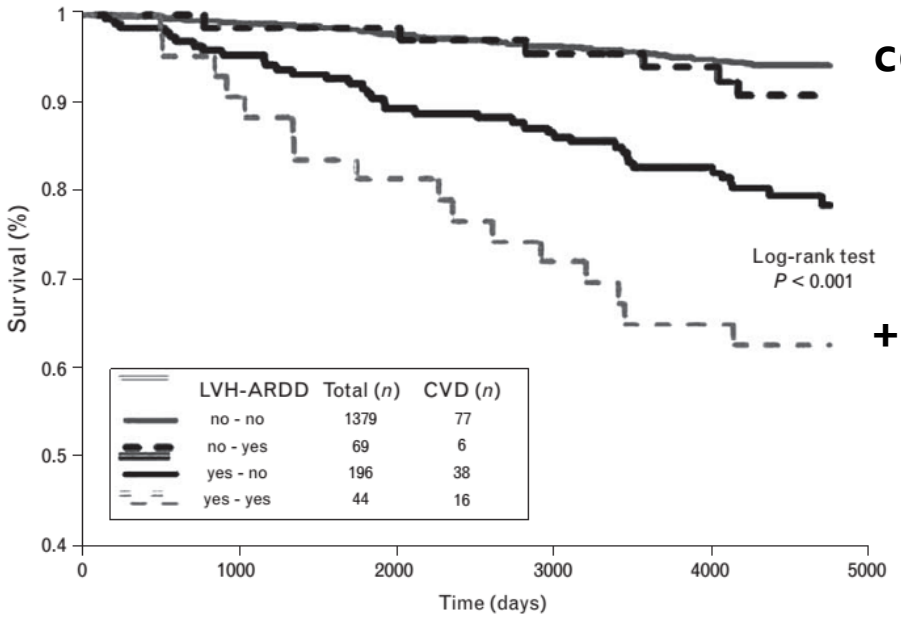




Elefteriades *JACC* 2010

Prognosis of LVH and ARD

Aortic root diameter and risk of cardiovascular events in a general population: data from the PAMELA study



controlli

+LVH + ARD

Cuspidi et al J of Hypertens 2014

Drugs to be preferred in specific conditions

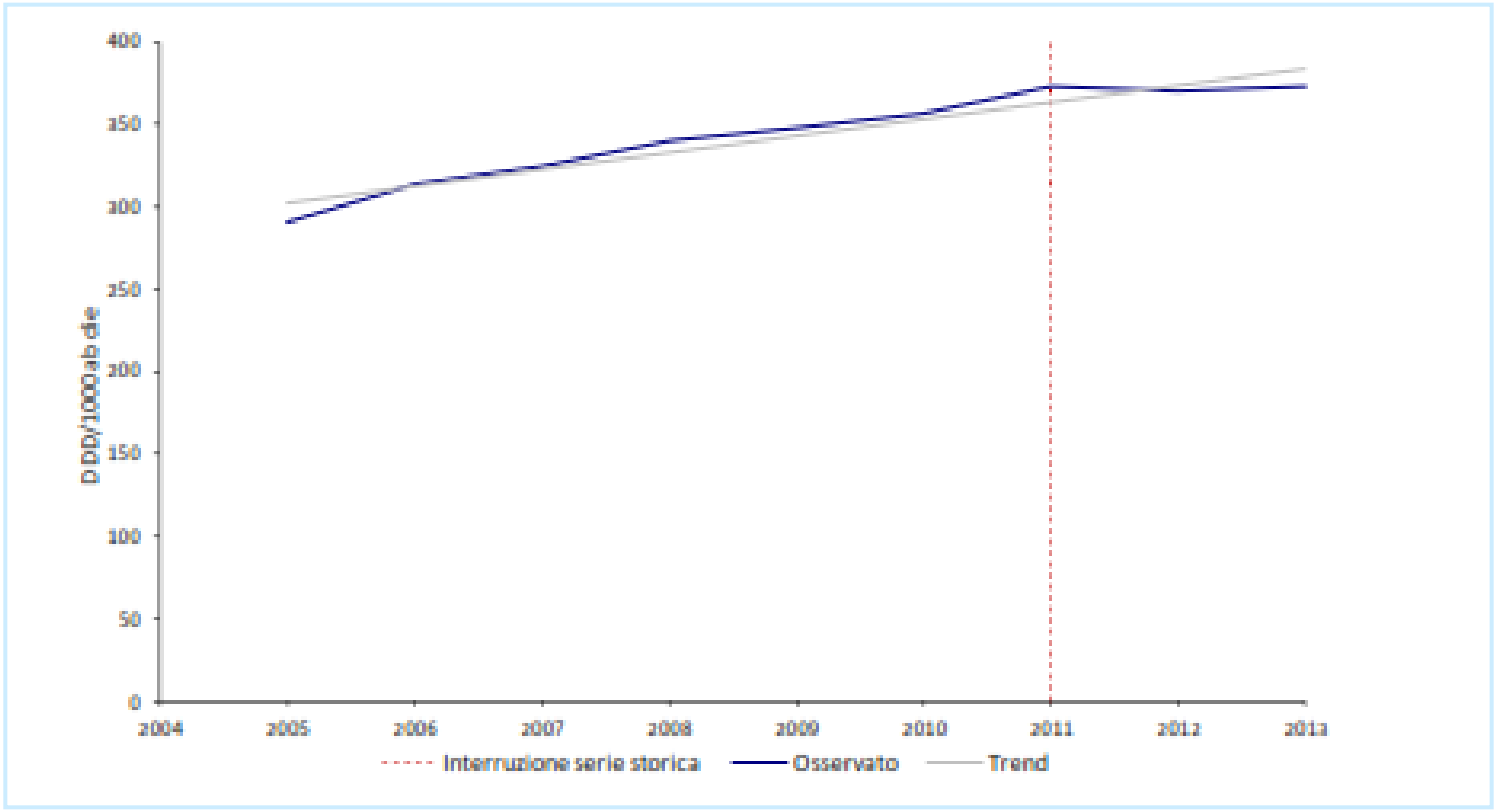
Condition	Drug
Asymptomatic organ damage	
LVH	ACE inhibitor, calcium antagonist, ARB
Asymptomatic atherosclerosis	Calcium antagonist, ACE inhibitor
Microalbuminuria	ACE inhibitor, ARB
Renal dysfunction	ACE inhibitor, ARB
Clinical CV event	
Previous stroke	Any agent effectively lowering BP
Previous myocardial infarction	BB, ACE inhibitor, ARB
Angina pectoris	BB, calcium antagonist
Heart failure	Diuretic, BB, ACE inhibitor, ARB, mineralocorticoid receptor antagonists
Aortic aneurysm	BB
Atrial fibrillation, prevention	Consider ARB, ACE inhibitor, BB or mineralocorticoid receptor antagonist
Atrial fibrillation, ventricular rate control	BB, non-dihydropyridine calcium antagonist
ESRD/proteinuria	ACE inhibitor, ARB
Peripheral artery disease	ACE inhibitor, calcium antagonist

2013 ESH/ESC Hypertension Guidelines

Farmaci per ipertensione e scompenso, andamento temporale del consumo (2005-2013)

Tabella 7.2.5b. Farmaci per l'ipertensione e lo scompenso, andamento regionale delle DDD/1000 abitanti die pesate: confronto 2005-2013

	2005	2006	2007	2008	2009	2010	2011*	2012	2013	Δ % 13-12
Piemonte	275,0	295,1	308,2	323,9	333,8	343,0	353,6	354,1	356,6	0,7
Valle d'Aosta	295,1	310,4	322,9	333,1	340,6	343,2	352,9	339,0	337,2	-0,5
Liguria	296,8	311,4	324,0	335,0	340,3	346,8	349,7	339,2	337,8	-0,4



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Farmaci per l'ipertensione e lo scompenso

	Spesa Totale (in milioni)	% su spesa SSN	DDD totali (milioni)
Angiotensina II antagonisti e diuretici	503,90	2,6	876,5
Angiotensina II antagonisti	434,00	2,2	1.227,1
Calcio antagonisti (diidropiridinici)	288,10	1,5	1.200,0
ACE inibitori	274,40	1,4	1.988,5
Beta bloccanti	269,90	1,4	906,8
ACE inibitori e diuretici	222,30	1,1	564,0
Alfa bloccanti periferici	76,00	0,4	170,9
Diuretici ad azione maggiore da soli o in associazione a diuretici risp. di K+	62,30	0,3	638,3
ACE inibitori e calcio antagonisti	55,80	0,3	108,4
Calcio antagonisti (non diidropiridinici)	35,30	0,2	84,9
Beta bloccanti e diuretici	33,00	0,2	126,2
Diuretici risp. di K+	29,00	0,1	88,6
Tiazidici e simili (incluse associazioni)	18,20	0,1	125,5
Altre sostanze ad azione sul sistema renina - angiotensina	11,40	0,1	12,5

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Experimental and Clinical Evidence-Based Effects of Antihypertensive Agents in HHD

Pharmacological Class	Decrease of Blood Pressure	Regression of LVH	Repair of Remodeling
Diuretics	Yes	Mild effect	Proven for torsemide
β-Blockers	Yes	Mild-moderate effect	Apparently not
α-Blockers	Yes	Mild effect	Untested
Calcium antagonists	Yes	Marked effect	Apparently not
ACE inhibitors	Yes	Marked effect	Yes
Angiotensin receptor blockers	Yes	Marked effect	Yes
Aldosterone antagonists	Yes	Mild-moderate effect	Apparently yes
Direct renin inhibitors	Yes	Marked effect	Untested

Diez, Hypertension 2010


Grazie