University of Turin
Department of Medical Sciences
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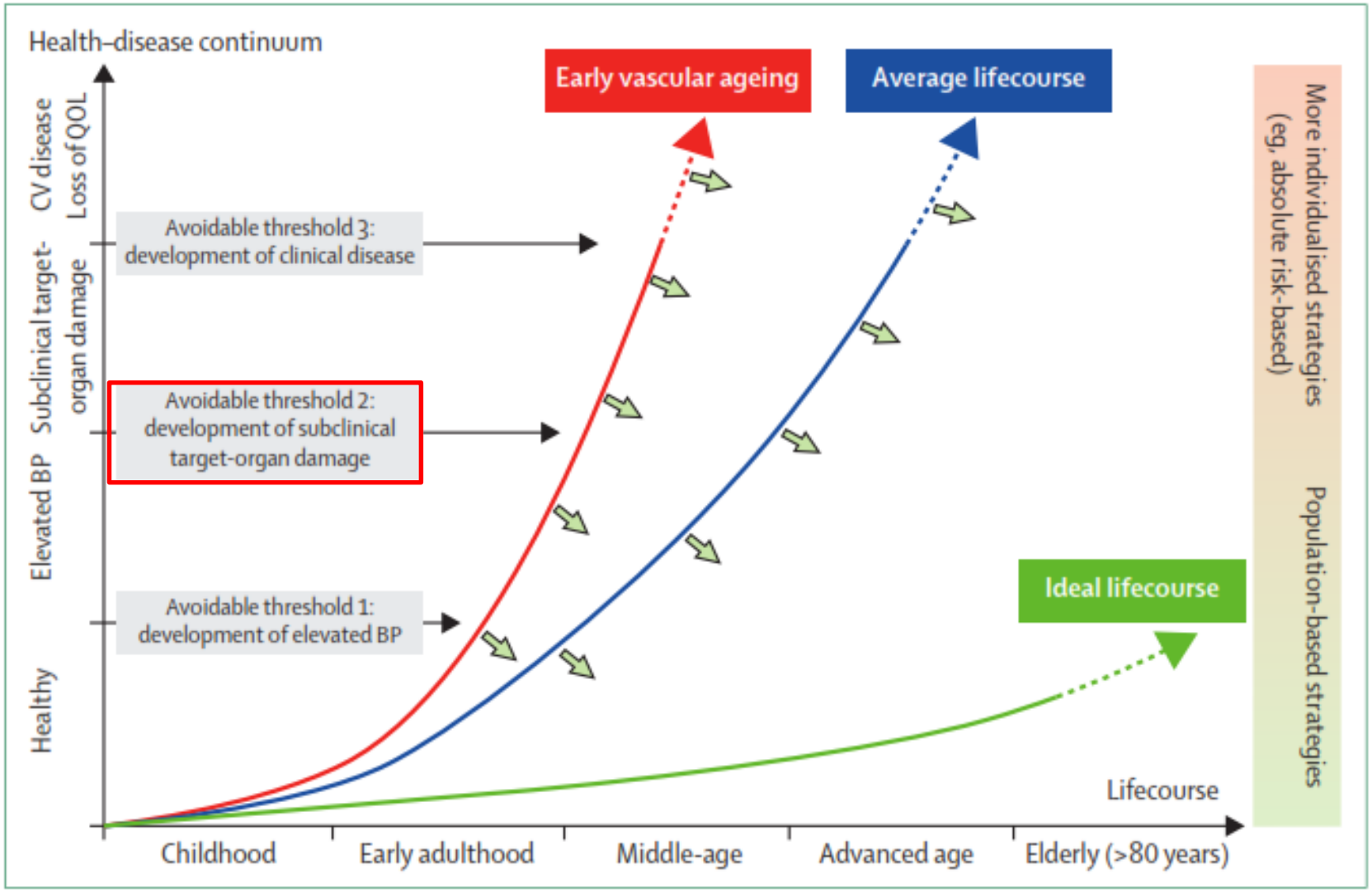
Internal Medicine and Hypertension Division
Turin

Hypertensive heart disease: overview, aetiology and epidemiology

Franco Veglio

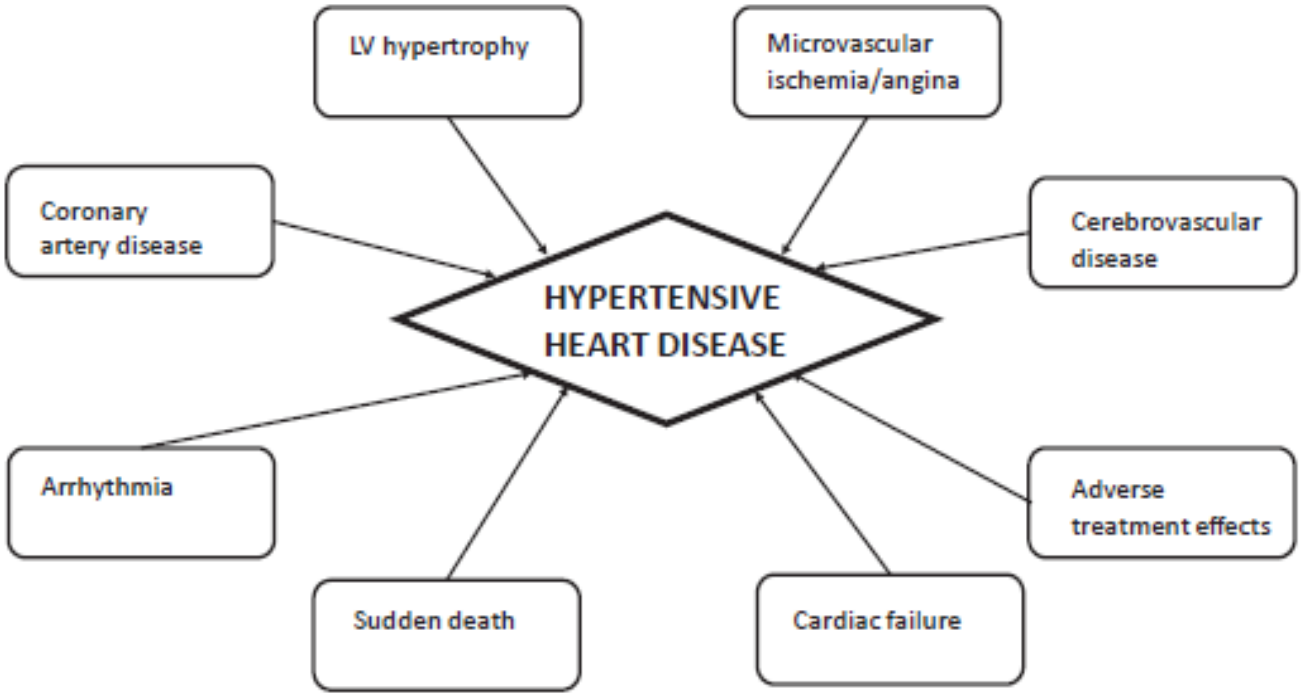
NO CONFLICTS OF INTEREST

The lifecourse approach to management of elevated blood pressure



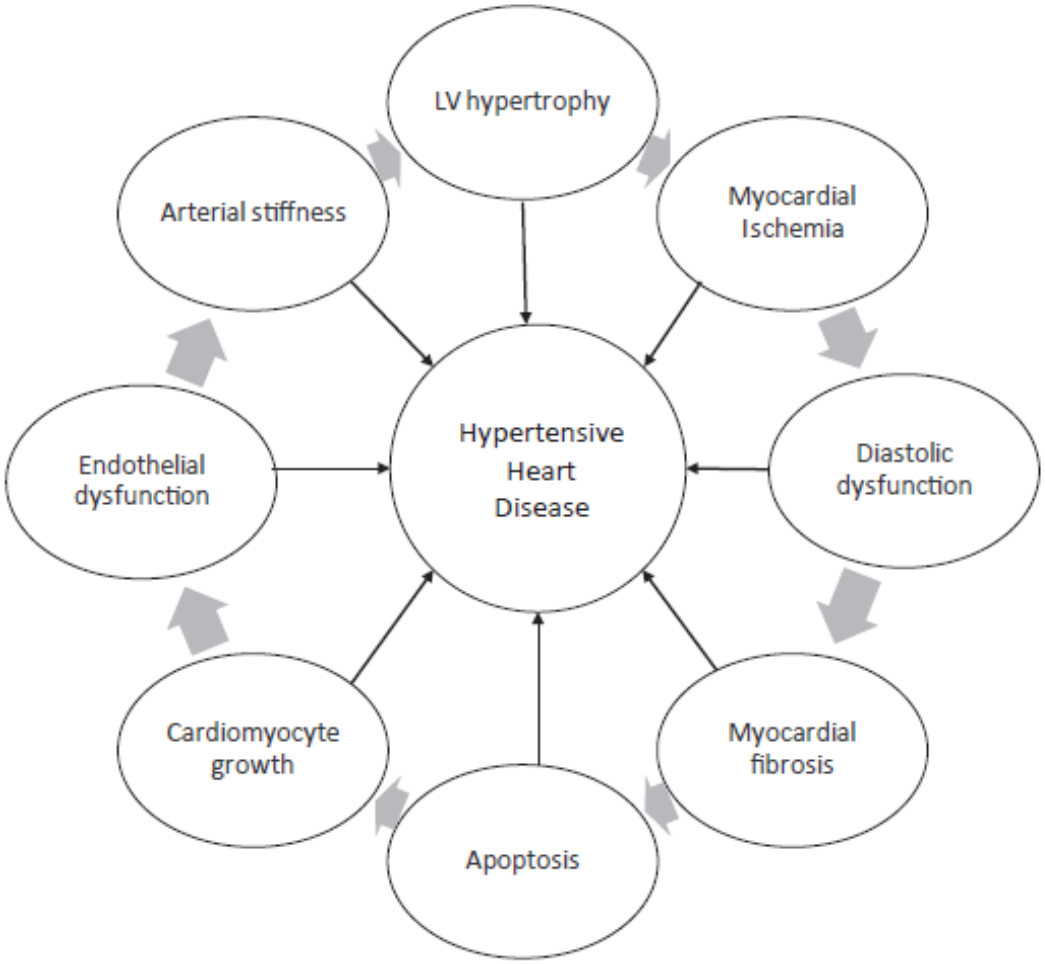
Holsen, Lancet 2016

The spectrum of risk conferred by HHD on cardiovascular morbidity and mortality



Stanton, Med Clin N Am, 2017

The maladaptive feedback of Hypertensive Heart Disease



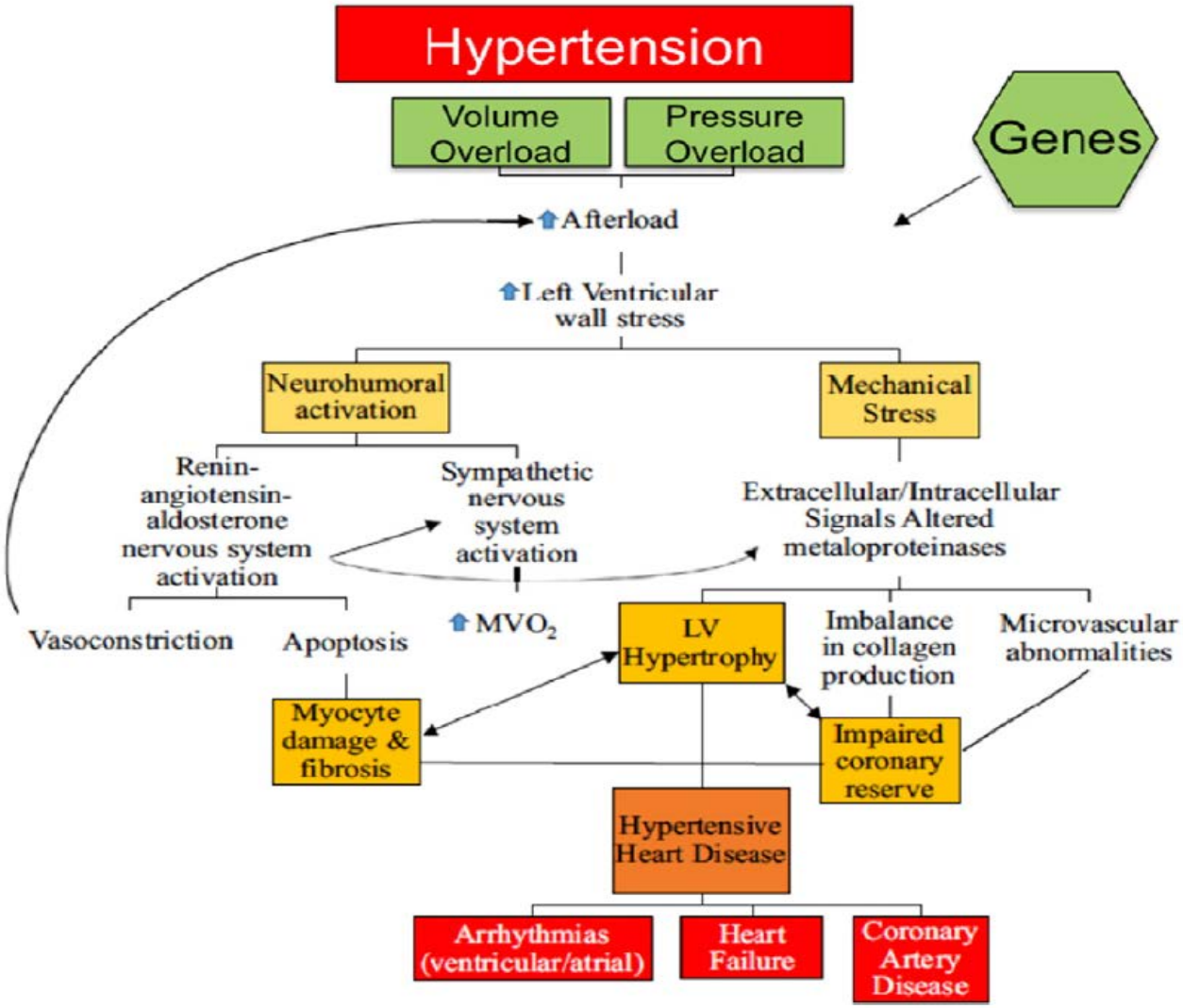
Stanton, Med Clin N Am, 2017

Factors in hypertensive heart disease resulting in ischemia

- Ventricular fibrosis with associated extraventricular ischemia
- Coronary arteriolar constriction due to fibrosis.
- Endothelial dysfunction of coronary resistance vessels
- Reduced coronary luminal area in relation to increased LV mass
- Increased LV wall tension
- Altered subendocardial-subepicardial blood flow ratio
- Impairment of diastolic coronary artery blood flow
- Decreased subendocardial capillary density
- Inflammatory responses

Stanton, Med Clin N Am, 2017

Pathophysiological pathways of hypertensive heart disease



Shenasa, Intern J Cardiol 2017

Changes of gene expression during cardiomyocyte hypertrophy

Genes whose expression is reactivated

β-Myosin heavy chain

Embryonic myosin light chain in ventricles

IVS3A form of calcium channel

α3-Subunit of Na^+, K^+-ATPase

Switch from fatty acid oxidation to glycolysis genes

Lactate dehydrogenase M subunits

B subunit of creatine kinase

Ventricular expression of atrial natriuretic factor

Genes directing cardiomyocyte lengthening

Genes whose expression is blunted

Calcium ATPase of sarcoplasmic reticulum (SERCA2)

β_1-Adrenergic receptors

M_2-Muscarinic receptors

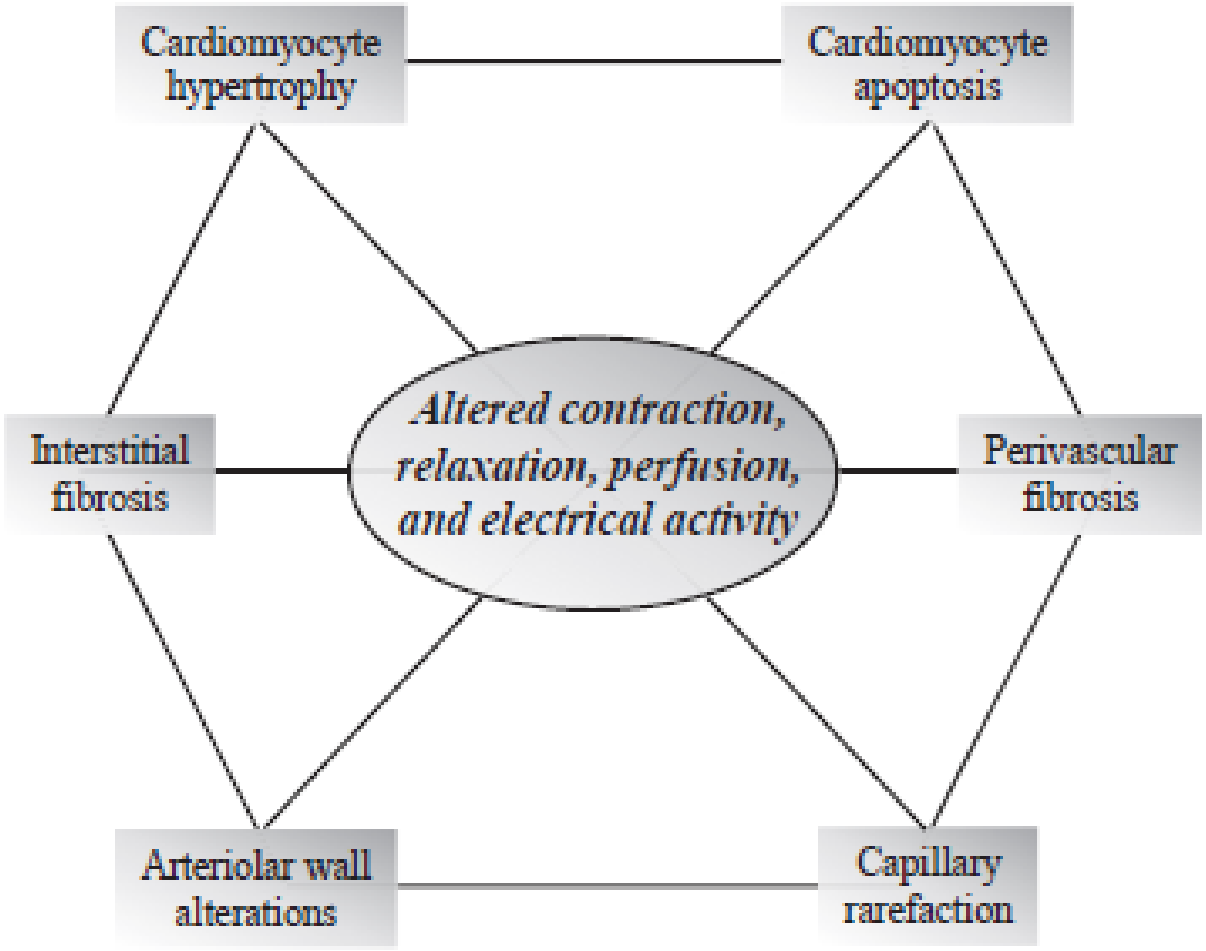
Early transient K^+ current, I_{to}

Myoglobin

N2BA titin isoform

Moreno, Med Clin N Am , 2017

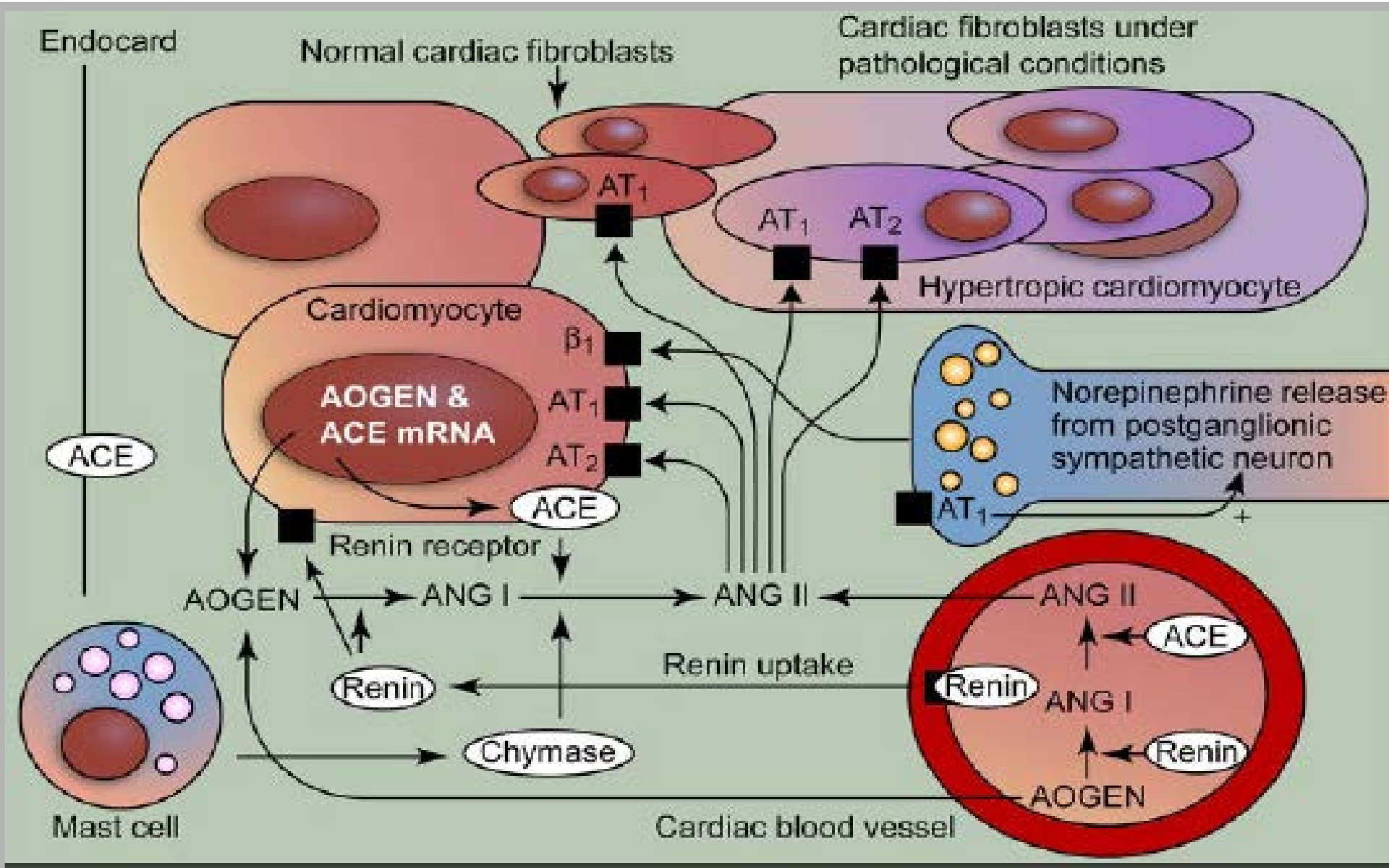
Mosaic of the histologic alterations in myocardium



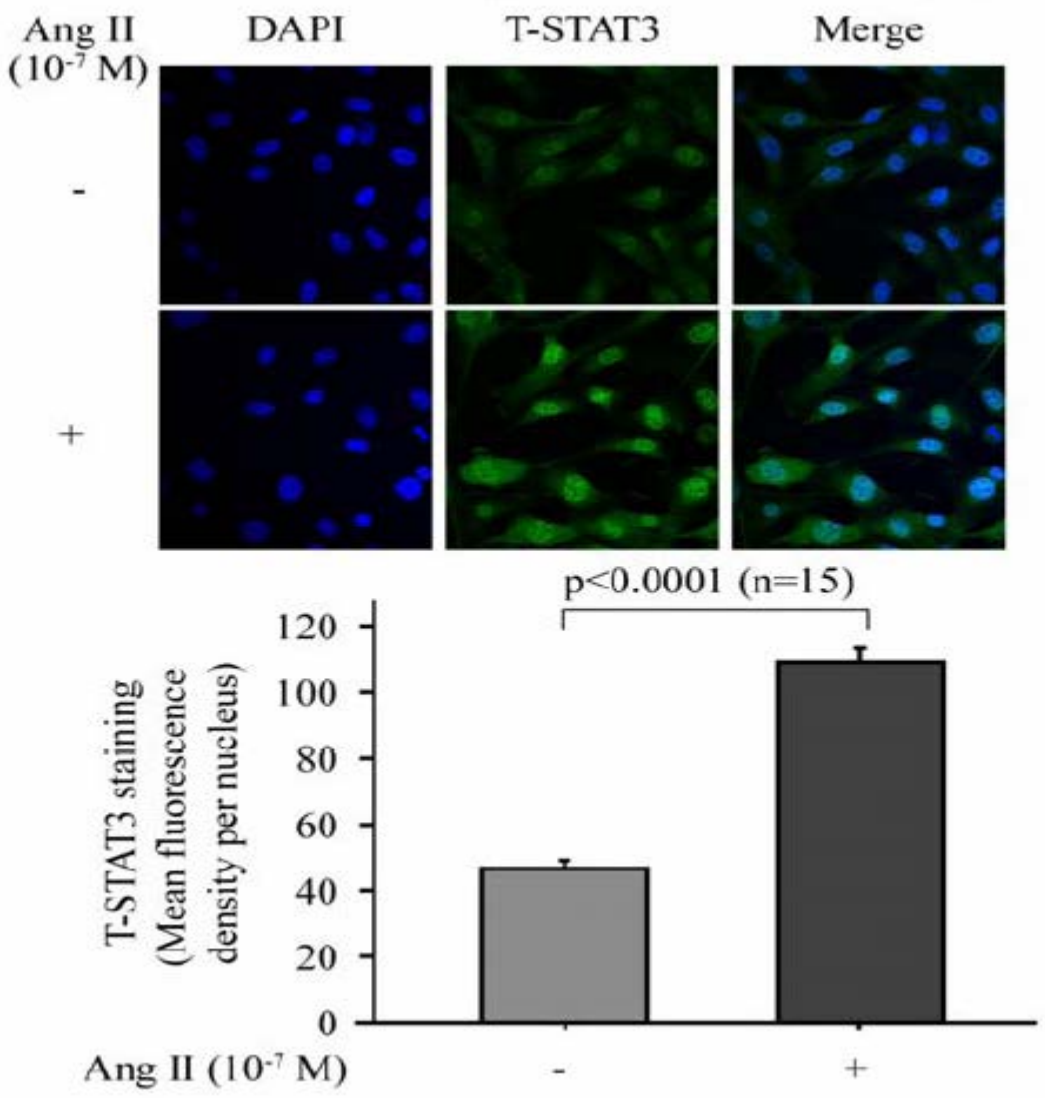
Moreno, Med Clin N Am , 2017

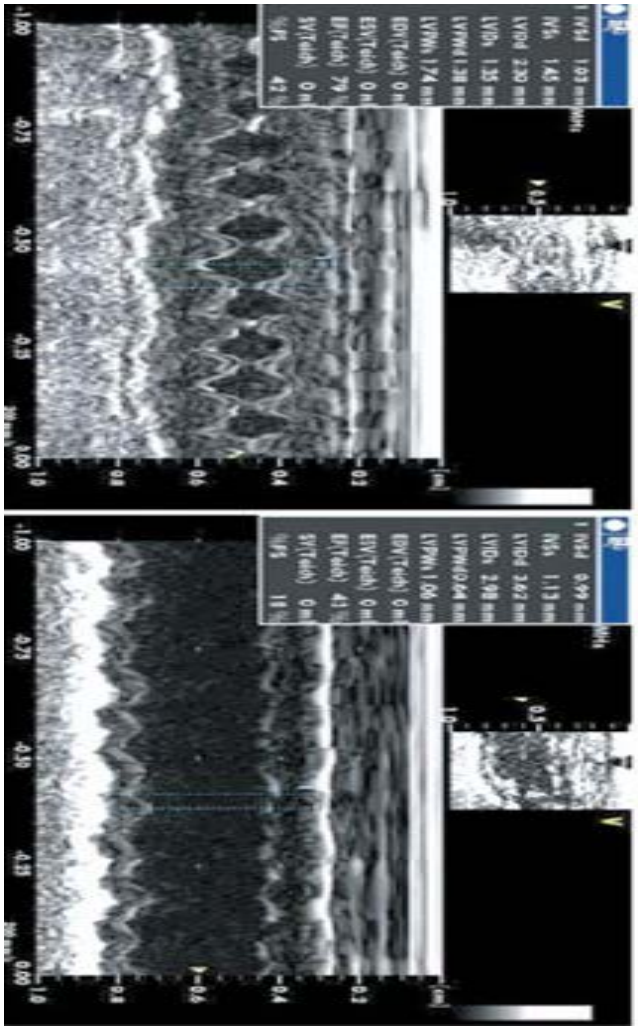
RAS & HEART

Paul, *Physiol Rev* 2006



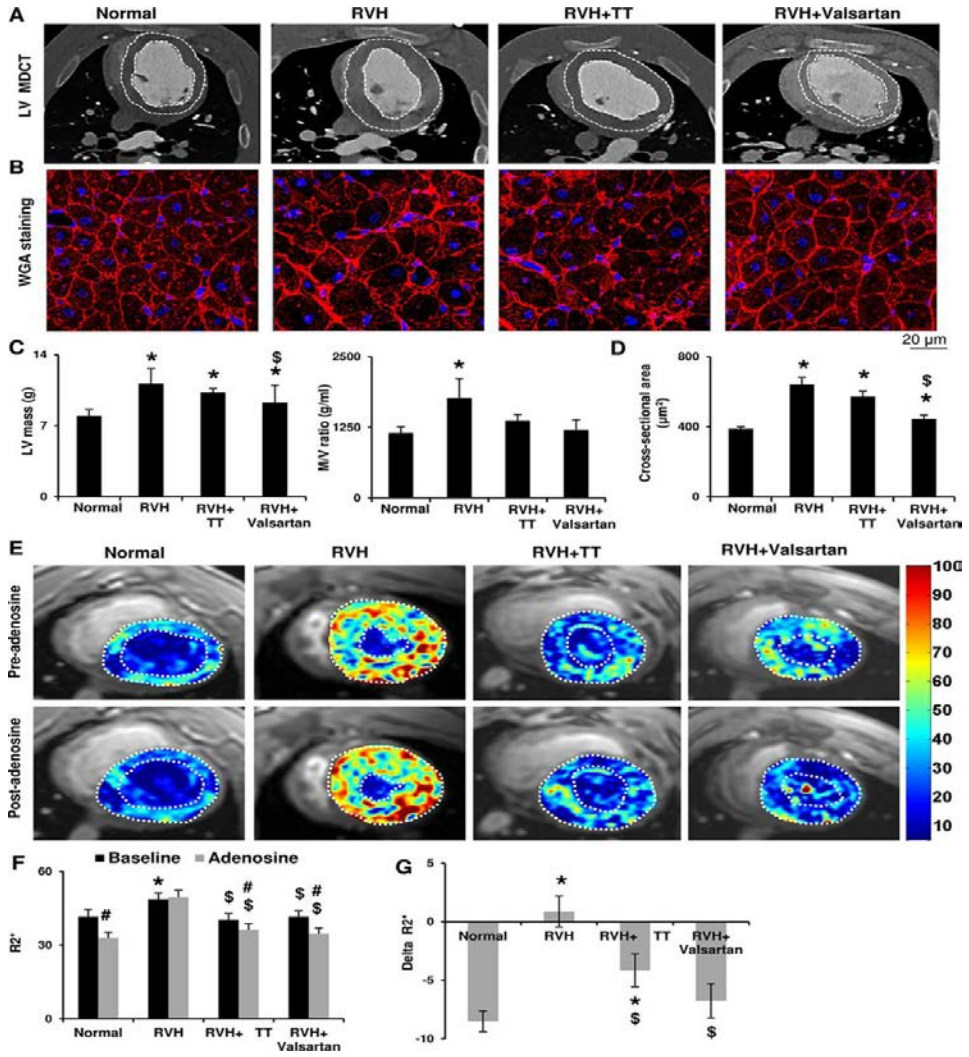
Role of nuclear unphosphorylated STAT3 in angiotensin II type 1 receptor-induced cardiac hypertrophy





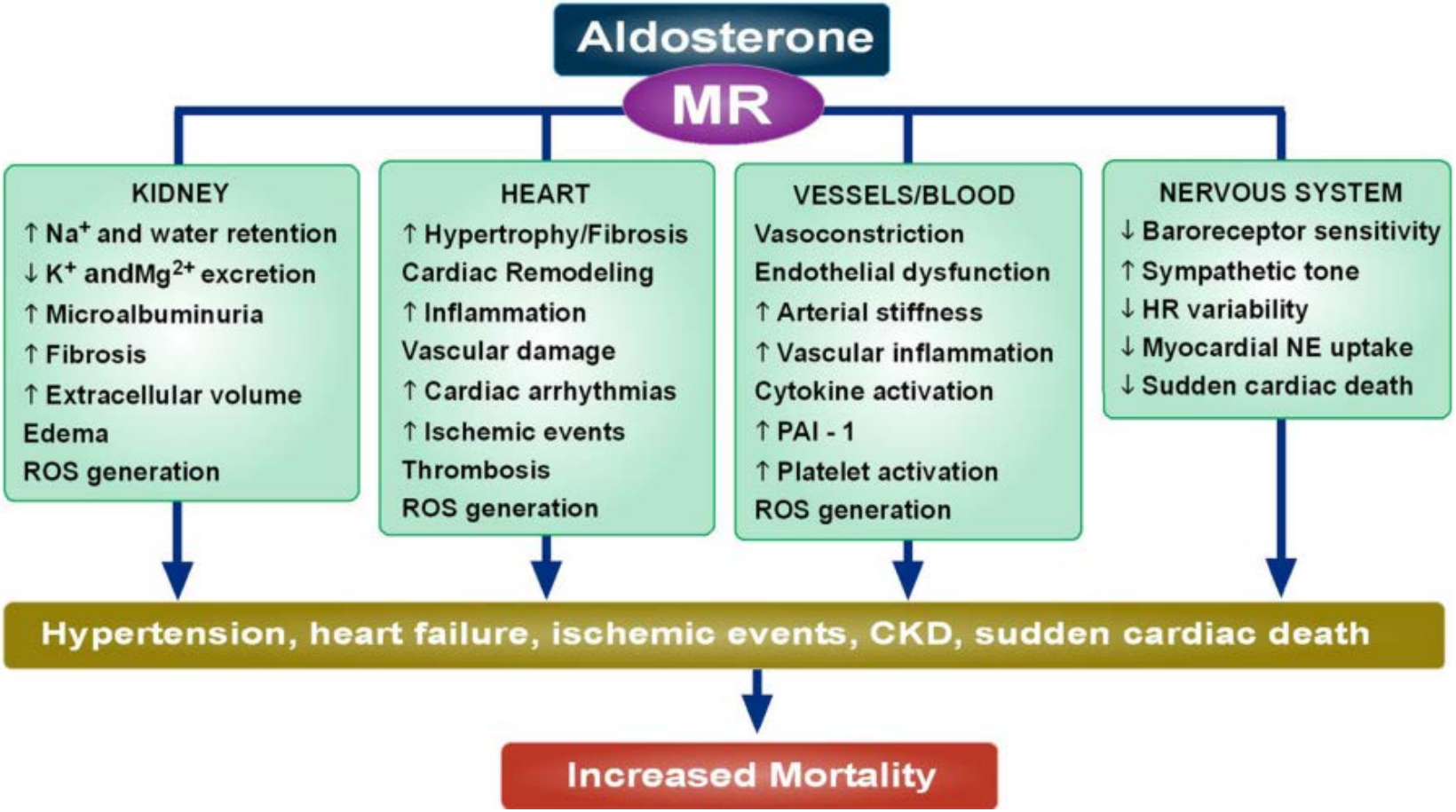
Yue, Cardiovascular Res Ad , 2009

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



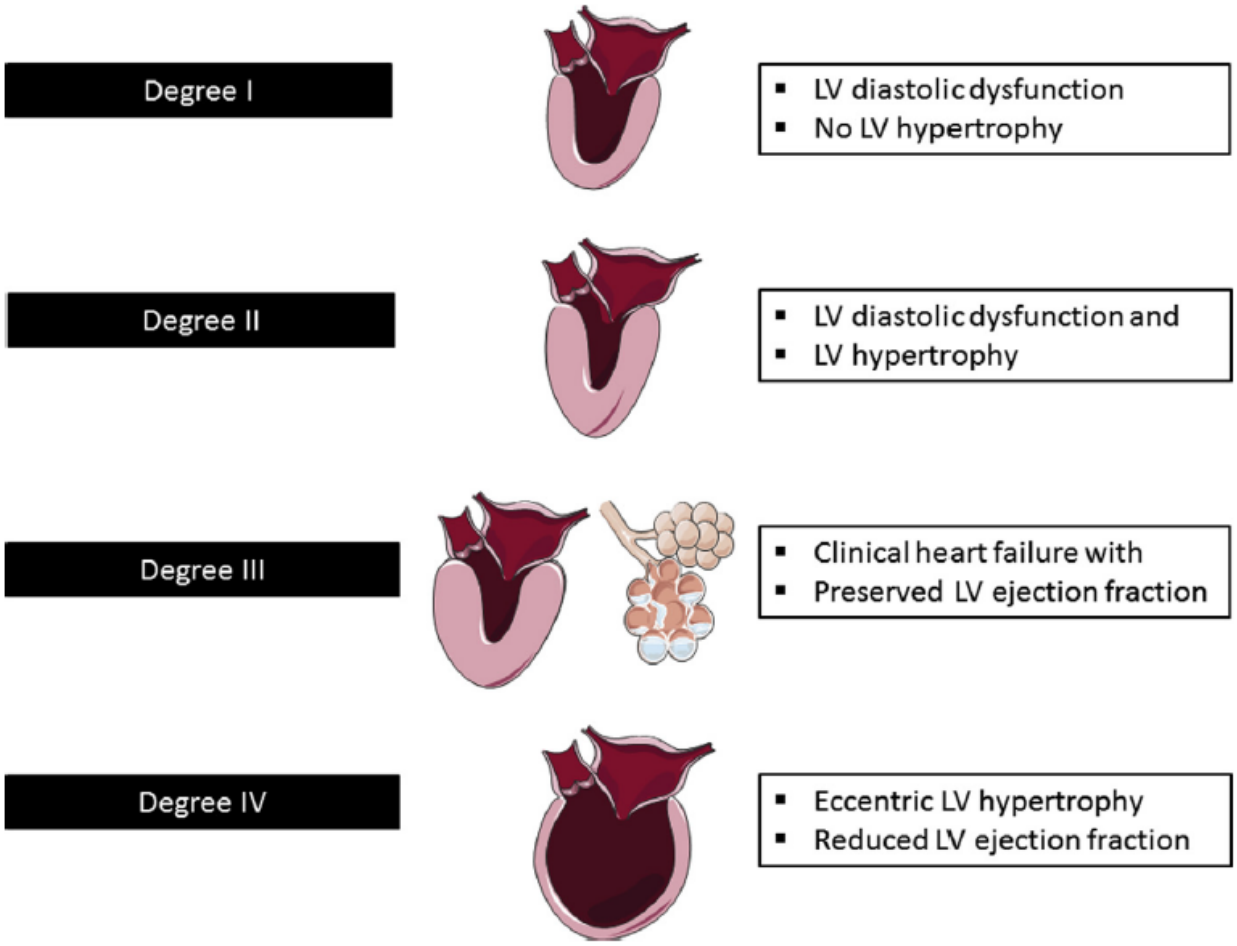
Zhang, Hypertension, 2014

Aldosterone and Heart



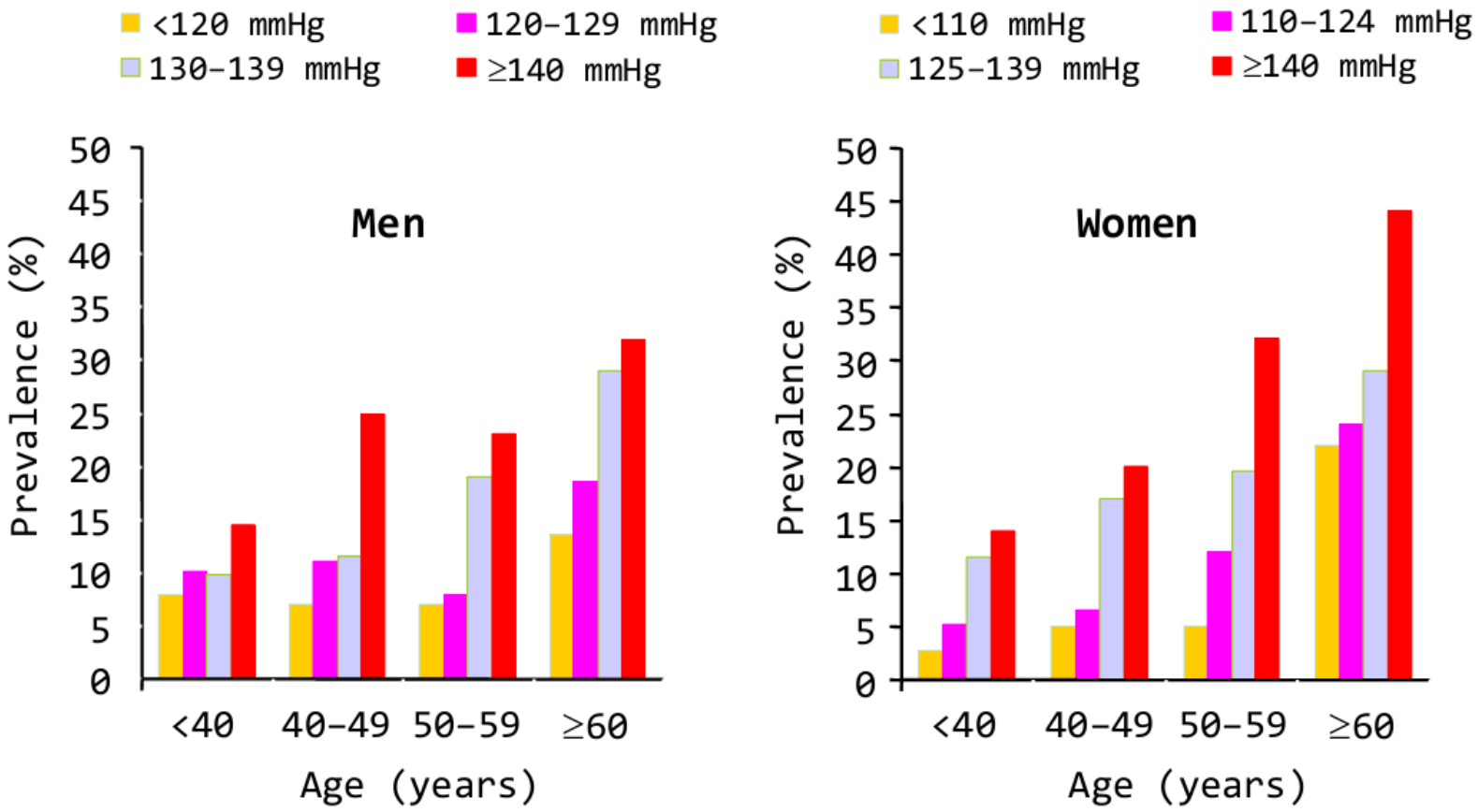
Tamargo, Sem Nephrol 2014

Staging of Hypertensive Heart Disease



Messerli, JACC 2017

Hypertension is a major risk factor for LVH



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

Prevalence of LVH

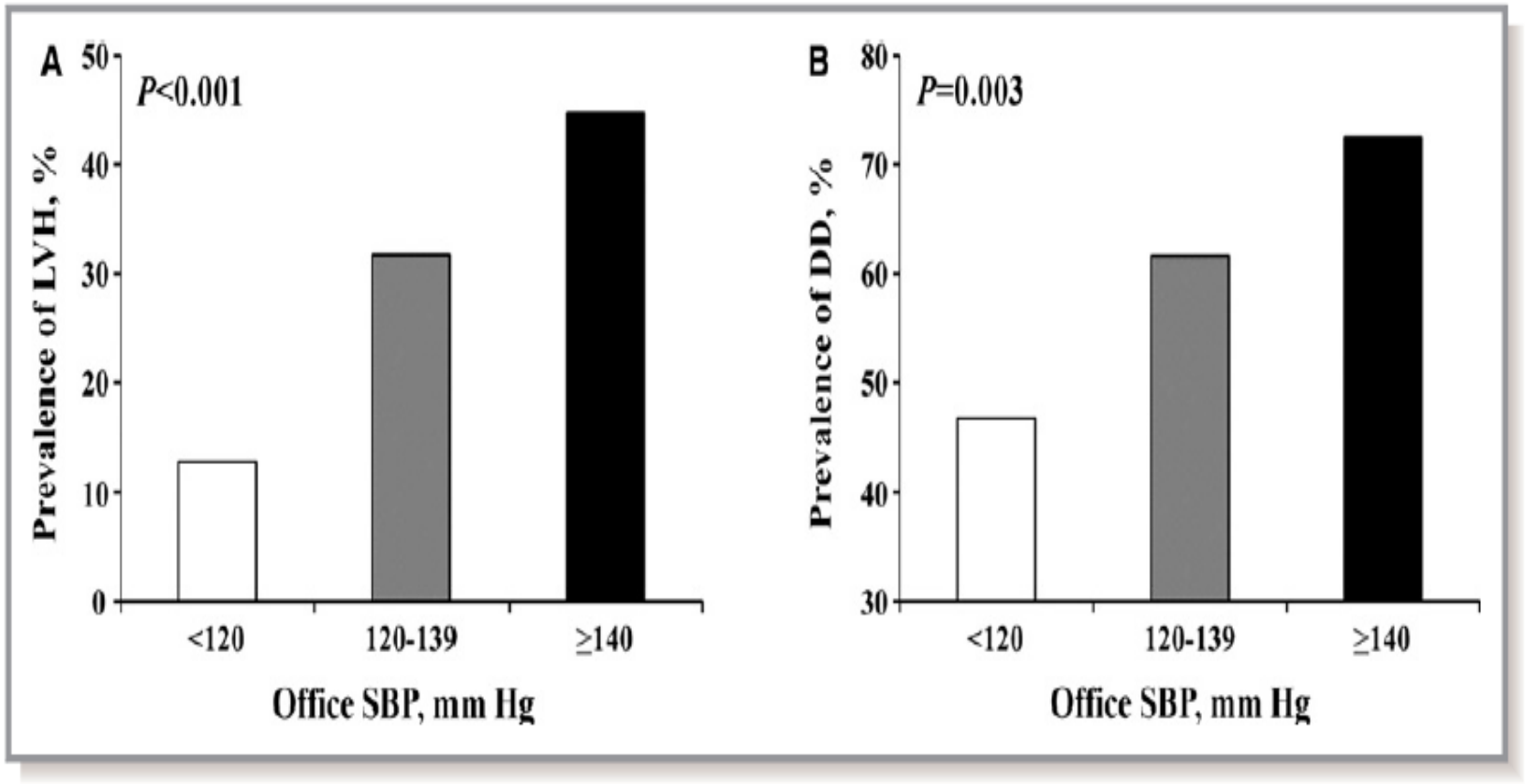
Author	ECG LVH criteria	ECHO LVH criteria	Prevalence of LVH (%)	
			ECG	ECHO
Verdecchia [13]	Wilson	LVMI >125 g/m^2	0.6	27.2
	LV strain	LVMI >51 gm$^{2.7}$	3.0	49.9
	Romhilt-Estes		4.8	
	Gubner Ungerleider		7.1	
	Sokolow -Lyon		11.1	
	Cornell voltage		11.9	
	Perugia score		18.4	
Salles [17]	Sokolow -Lyon, 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, J of Hypertens, 2012

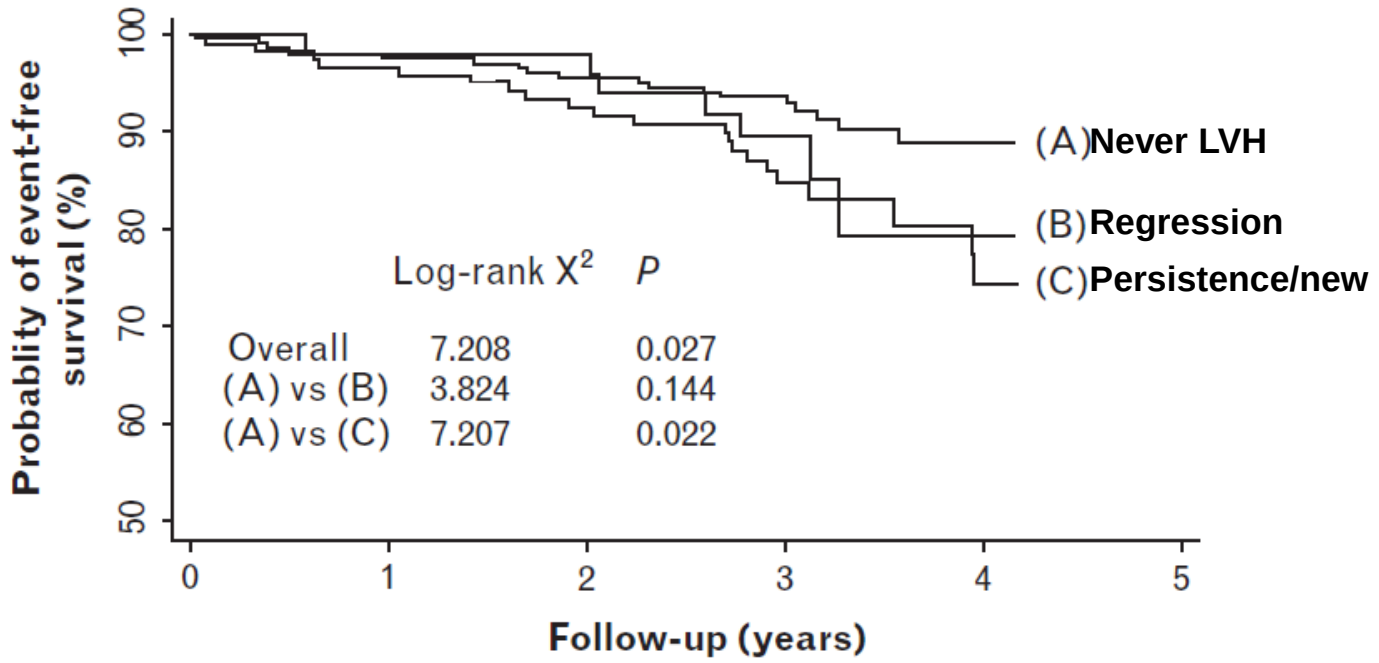
Prevalence of left ventricular hypertrophy (LVH)



Nakanishi, J Am Heart Assoc 2017

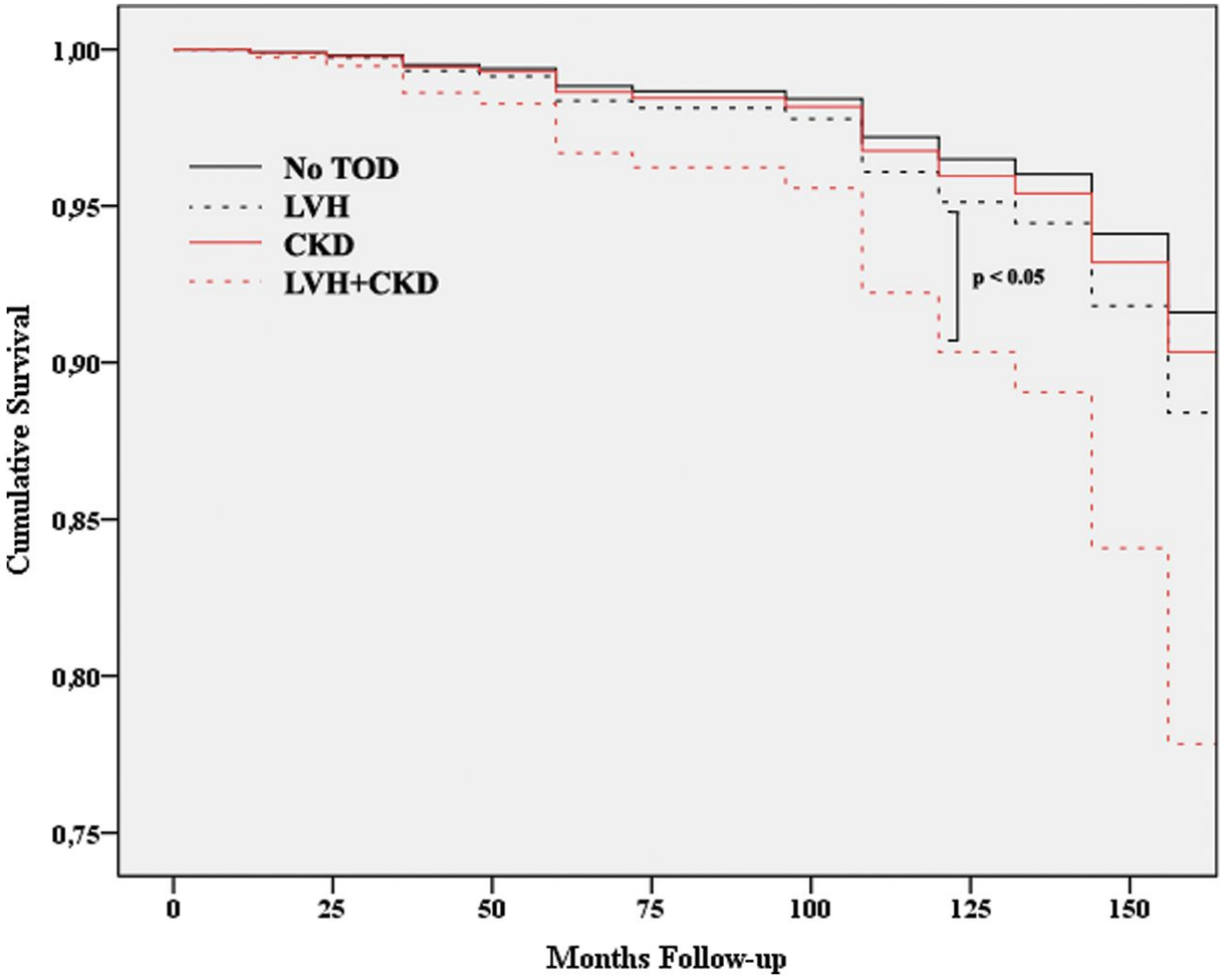
The prognostic legacy of left ventricular hypertrophy: cumulative evidence after the MAVI study

LVM measured at baseline and 2 years after the initial assessment in 374 patients. FU after 2nd vis 3.2 yrs.



Angeli, Journal of Hypertension 2015

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



Carpinella, Am J Hypertens 2014

Risk Reduction After Regression of Echocardiographic Left Ventricular Hypertrophy

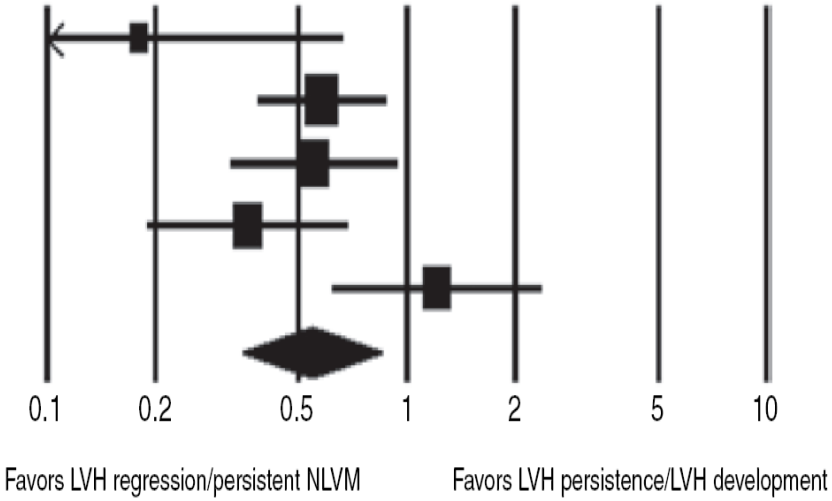
(3,149 patients)

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

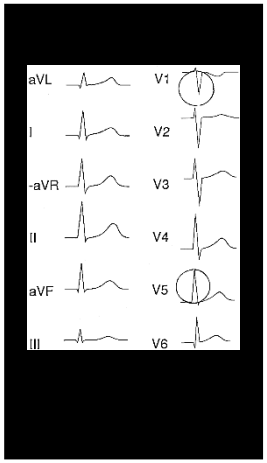
Statistics for each study

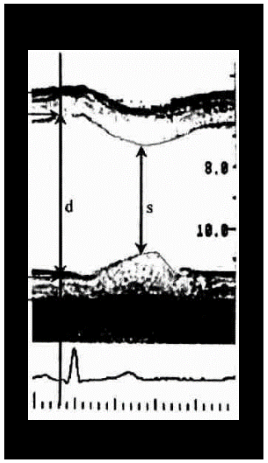
Hazard ratio and 95% CI

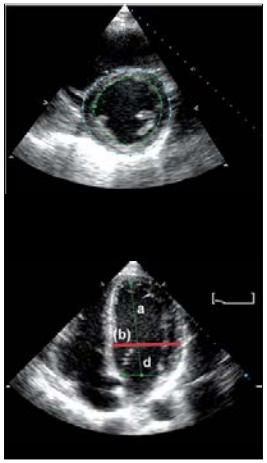


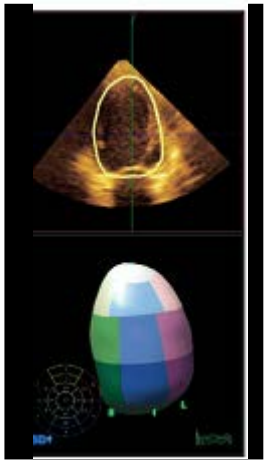
Pierdomenico, Am J Hyperten 2010

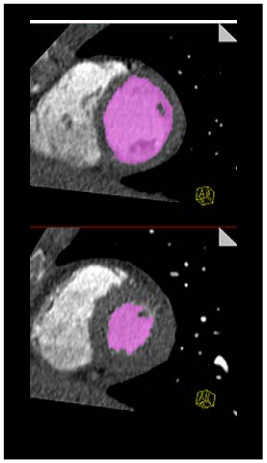
Methods of assessing hypertensive cardiomiopathy











	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

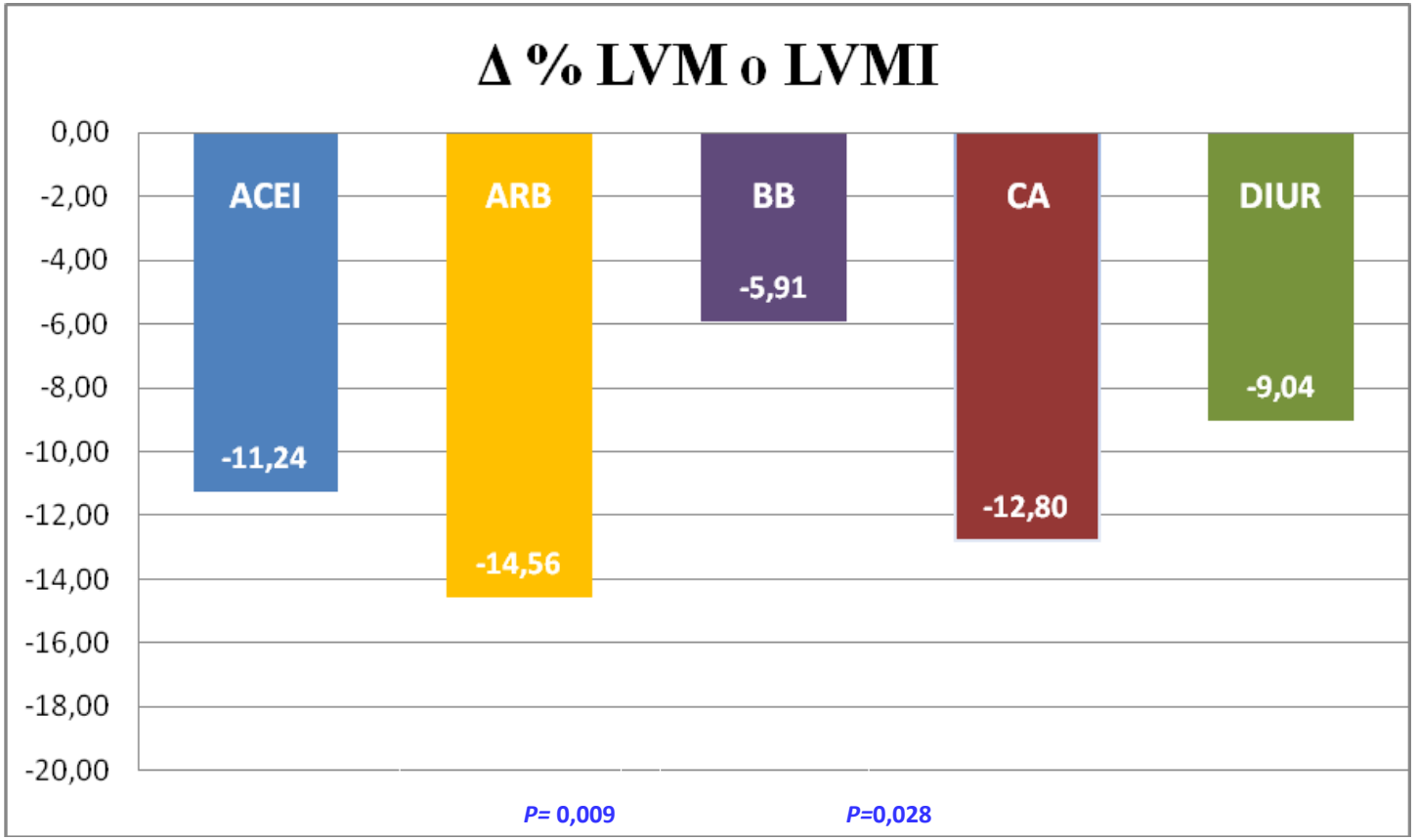
Ruilope Am J Hypert 2008

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

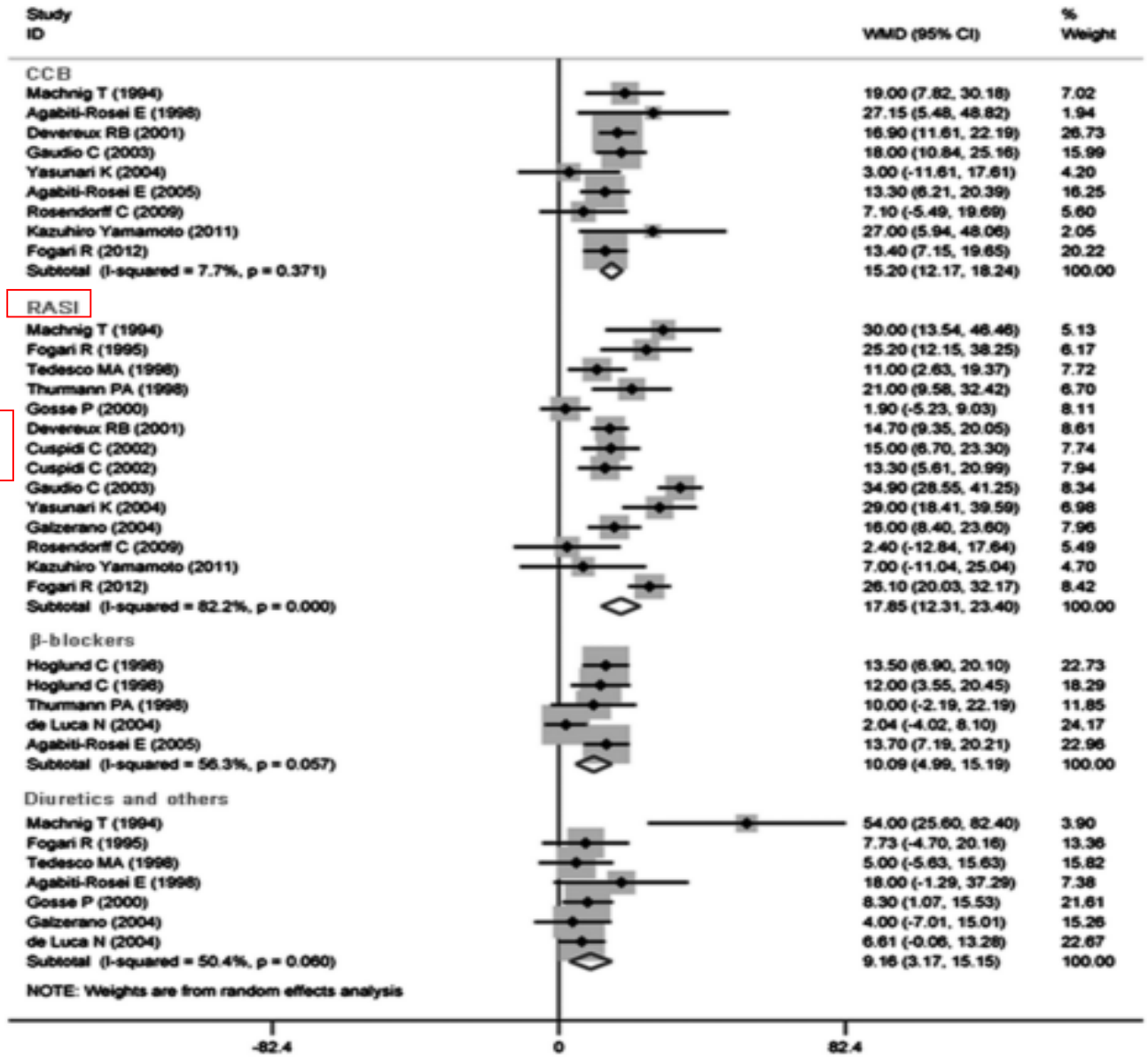
Metanalysis of echocardiographic studies on LVH regression



38 studies, 4227 patients

Muiesan, ESH 2010

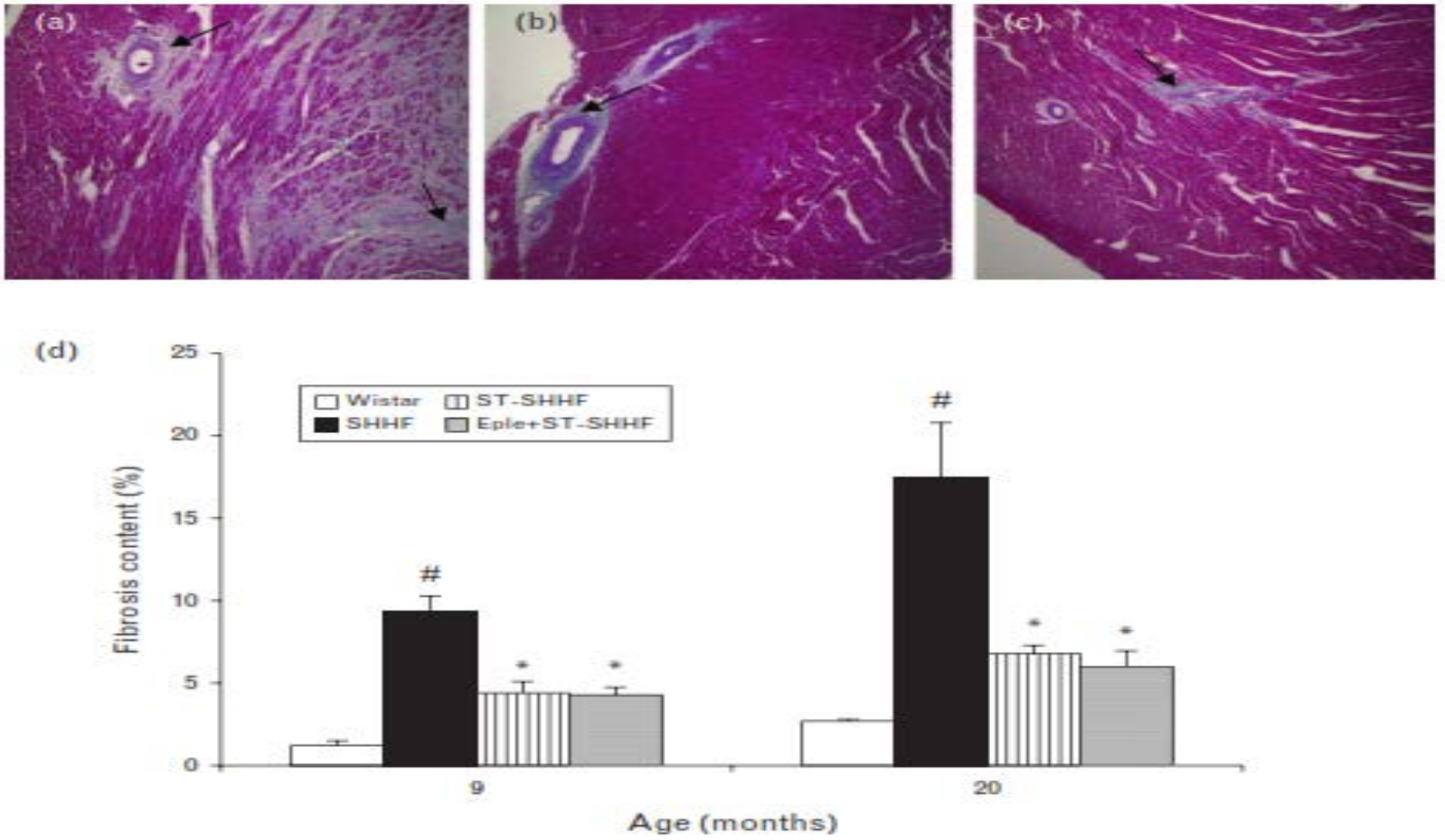
LVH and RAS inhibitors



-17.85 g m^{-2}

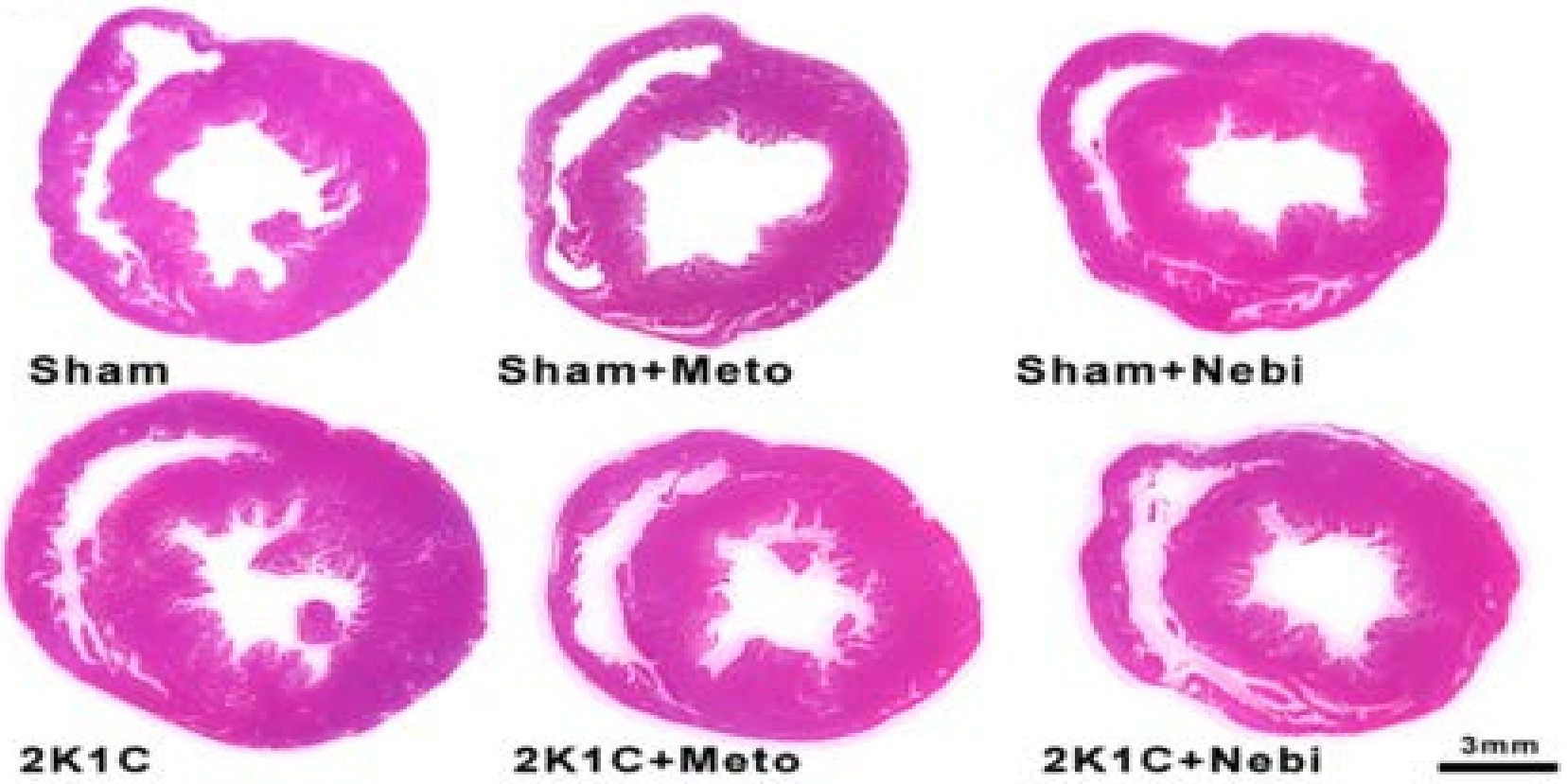
Zang, J H Hyperten 2013

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



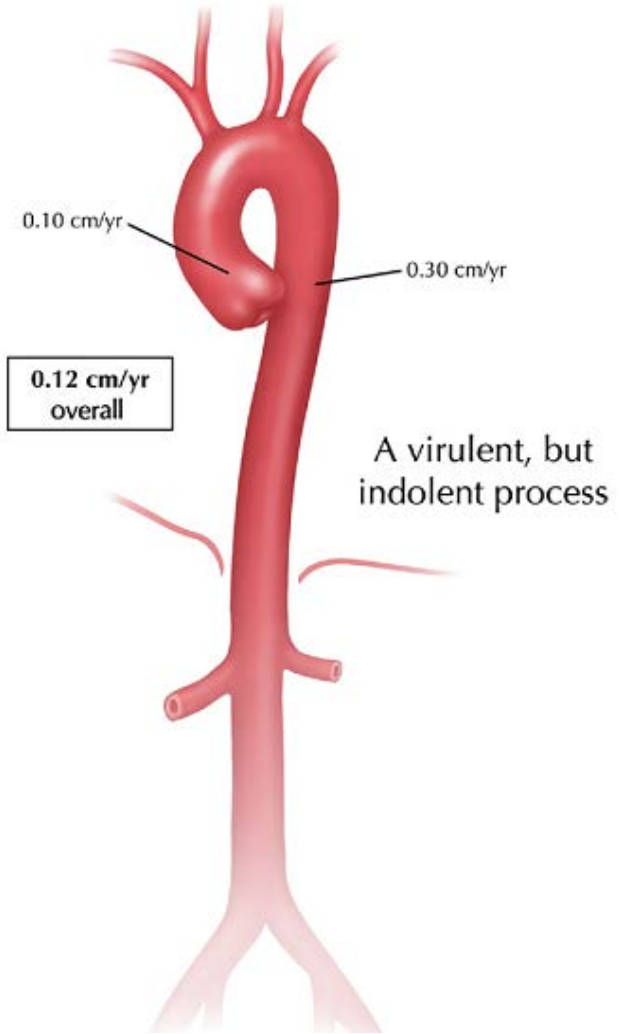
Munoz-Pacheco, J Hypertension 2013

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

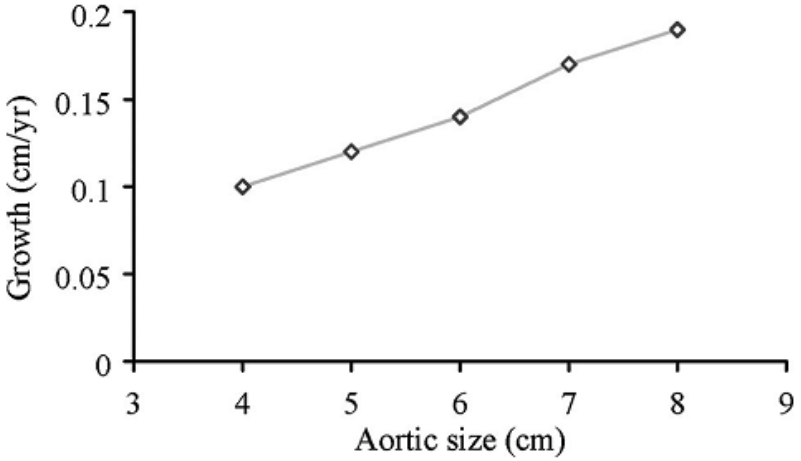


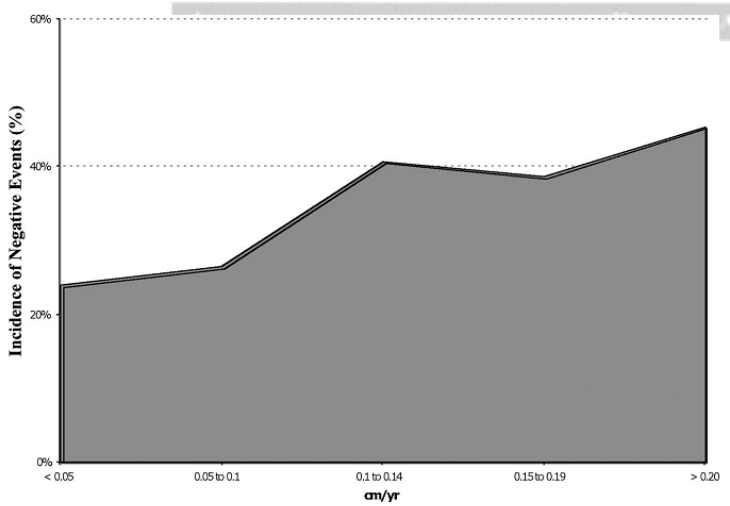
Rizzi, Free Rad Biol Med, 2014

Increasing by age



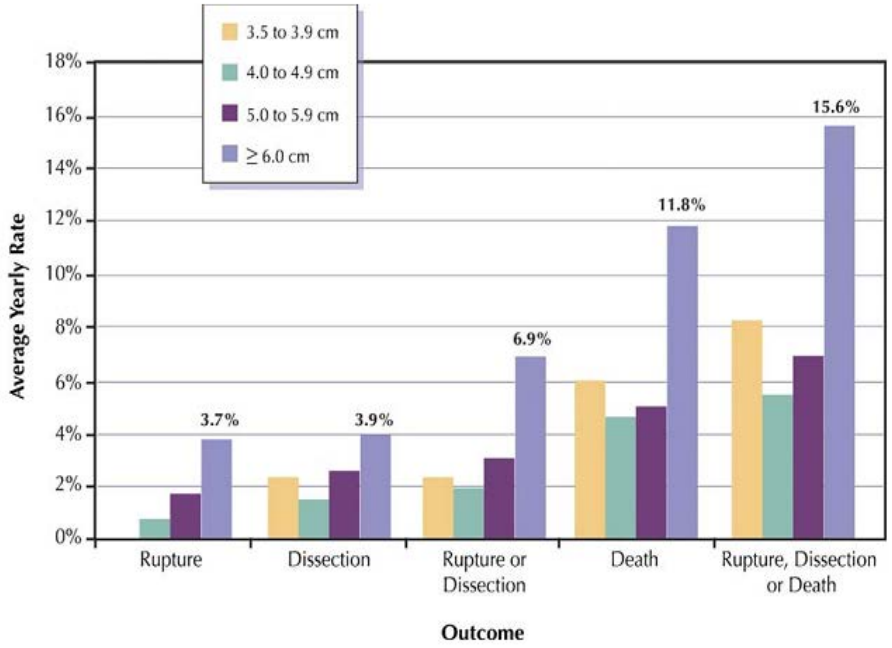
Elefteriades *JACC* 2010

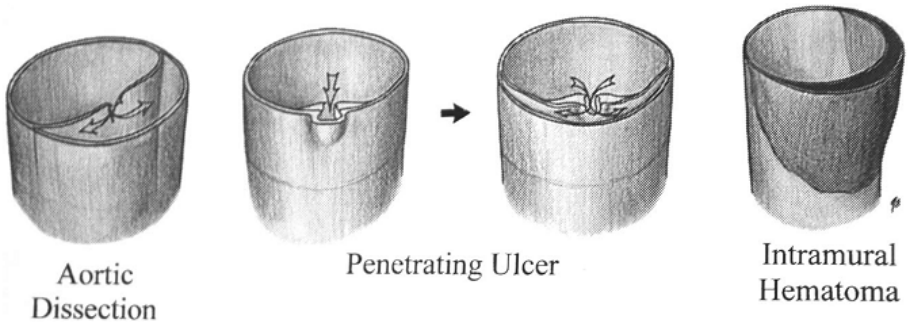




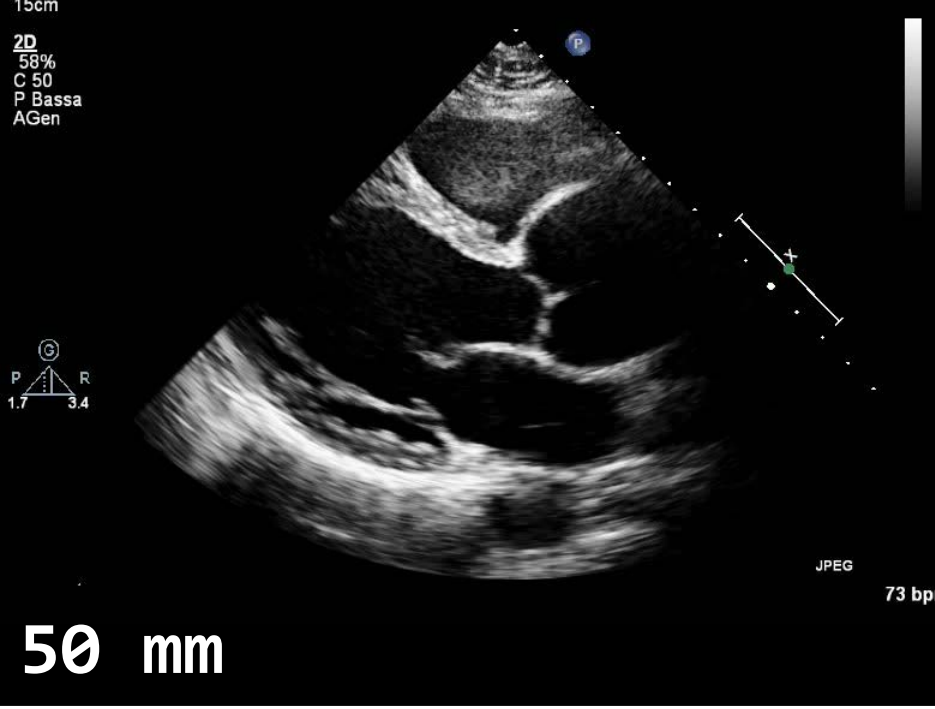
Coady et al. *Circulation* June 2010

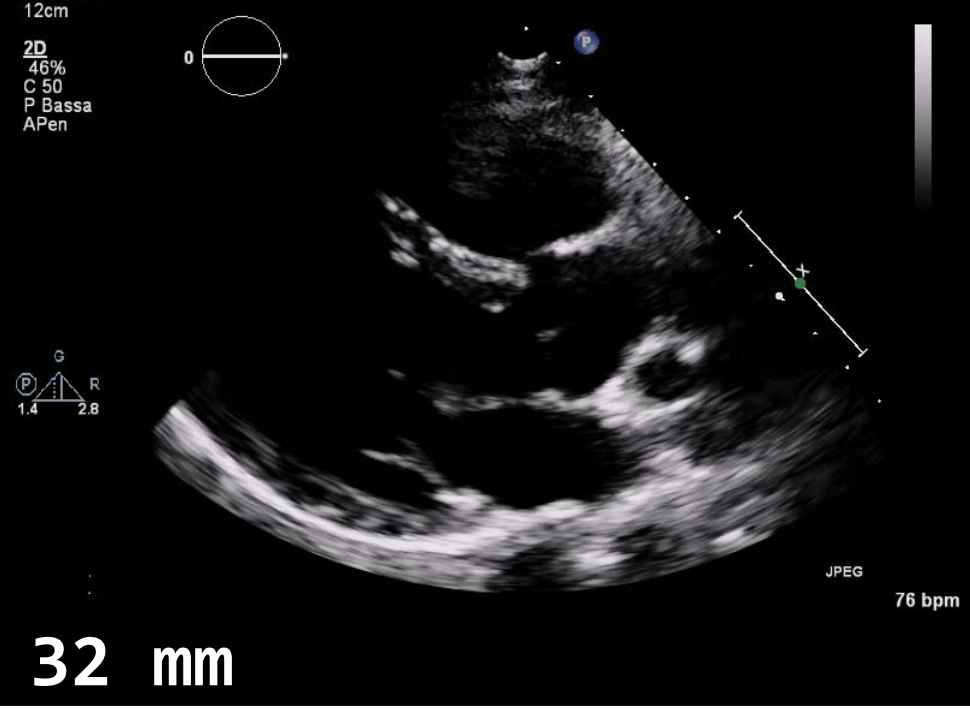
Prognosis





Elefteriades *JACC* 2010





Prevalence

9.1 %

12% males

4% females

Valsalva sinuses

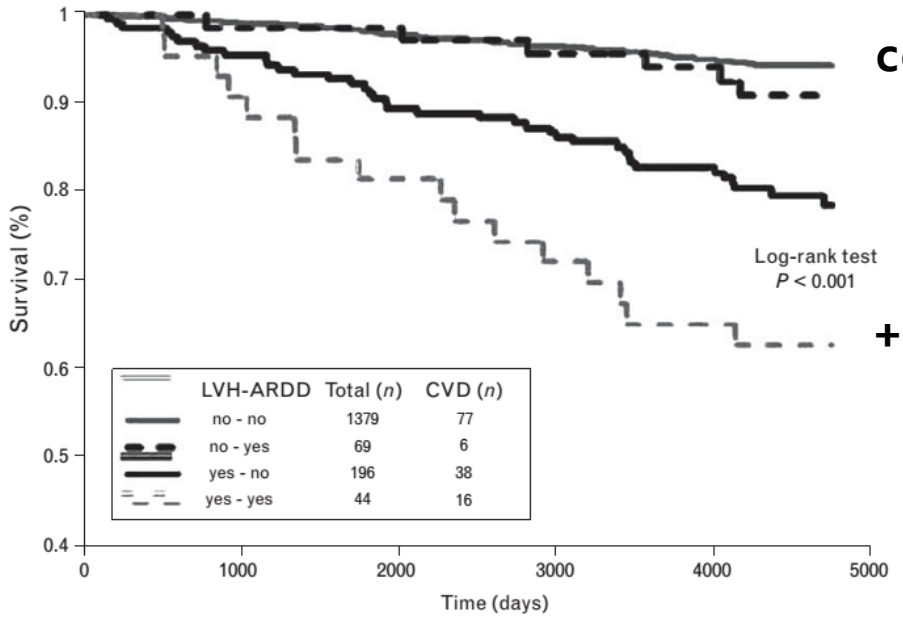
Echocardiographic aortic root dilatation in hypertensive patients: a systematic review and meta-analysis

Michele Covella[a,*], Alberto Milan[a,*], Silvia Totaro[a], Cesare Cuspidi[b], Annalisa Re[b], Franco Rabbia[a], and Franco Veglio[a]

J of Hypertens 2014

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

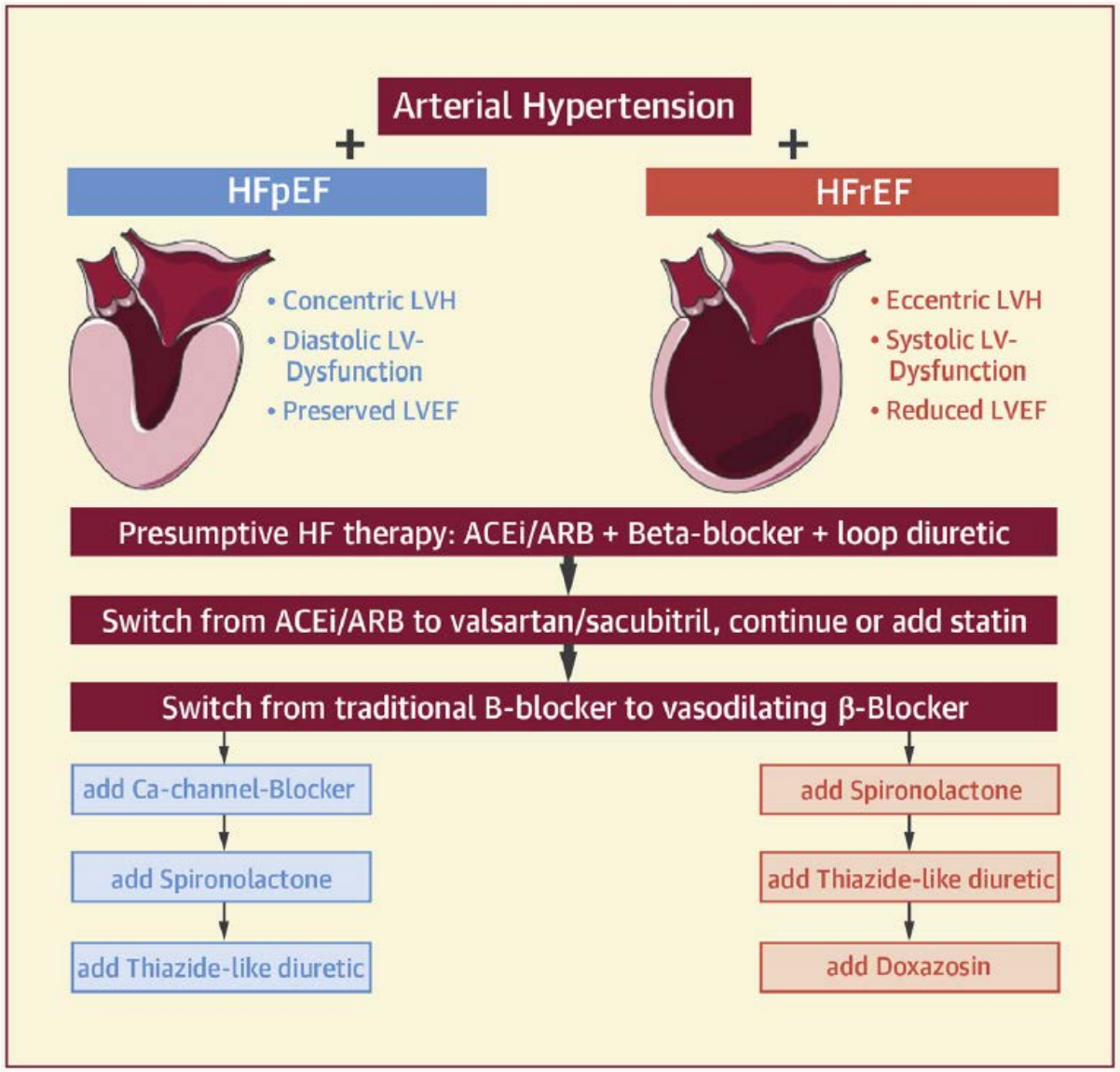
2013 ESH/ESC Hypertension Guidelines

Effects of Antihypertensive Agents in Hypertensive Heart Disease

Pharmacologic Class	Decrease of Blood Pressure	Reduction of LV Mass	Repair of Remodeling Lesions[a]
Diuretics	Yes	Mild	Proven for torasemide[44]
β-Blockers	Yes	Mild to moderate	Apparently not
α-Blockers	Yes	Mild	Unknown
Calcium antagonists	Yes	Moderate	Apparently not
Angiotensin-converting enzyme inhibitors	Yes	Marked	Proven for lisinopril[46]
Angiotensin receptor blockers	Yes	Marked	Proven for losartan[47]
Aldosterone antagonists	Yes	Mild-moderate	Proven for spironolactone[48]
Direct renin inhibitors	Yes	Marked	Unknown
Angiotensin receptor blocker and neprylisin inhibitor	Yes	Unknown	Unknown

Moreno, Med Clin N Am , 2017

Antihypertensive Strategy in Heart Failure Patients With Hypertension



Messerli, JACC 2017


Grazie