Assessment of Myocardial Aging and Atherosclerosis

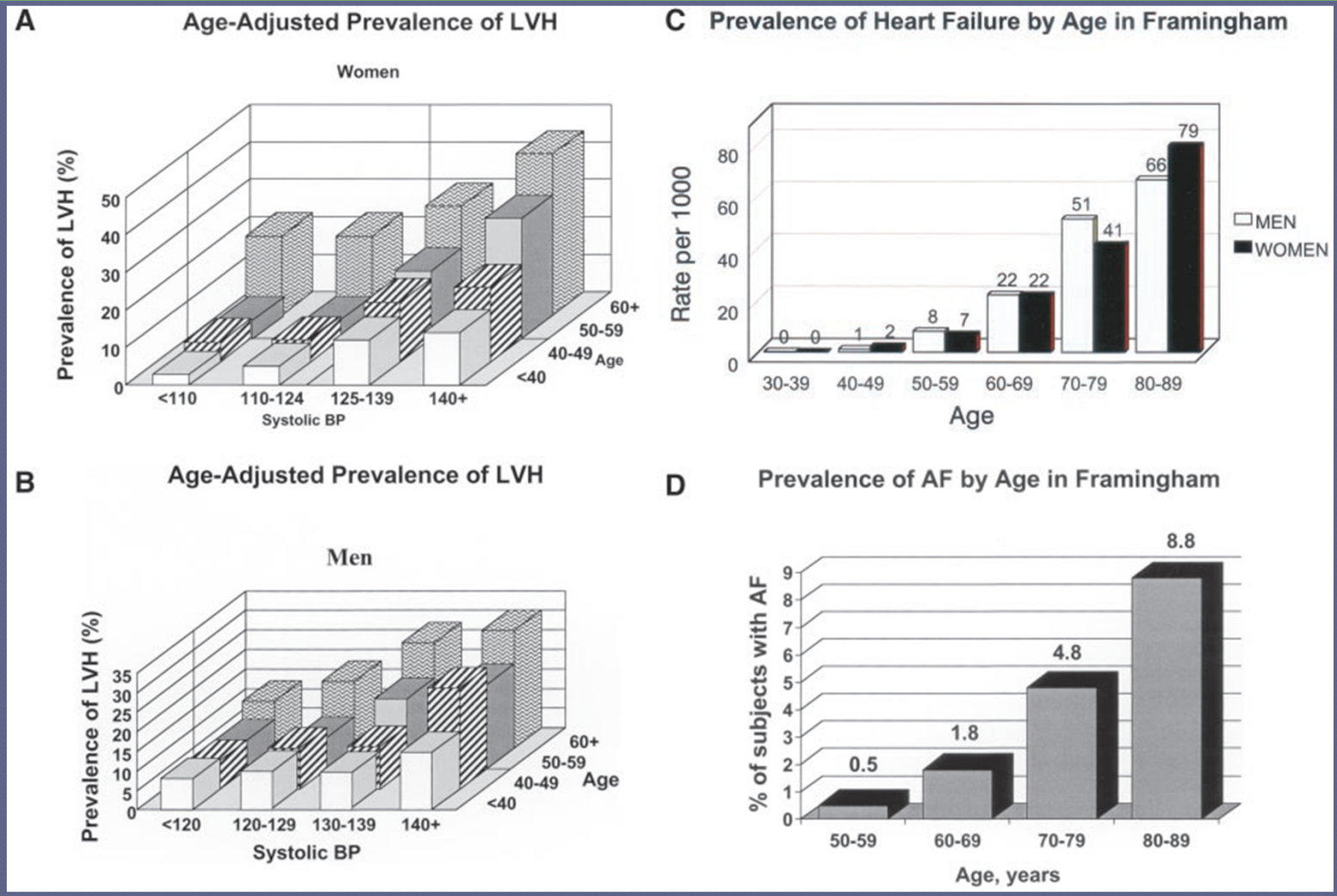
한림의대 강동성심병원

박 대 균

CardioVascular aging is disease ?

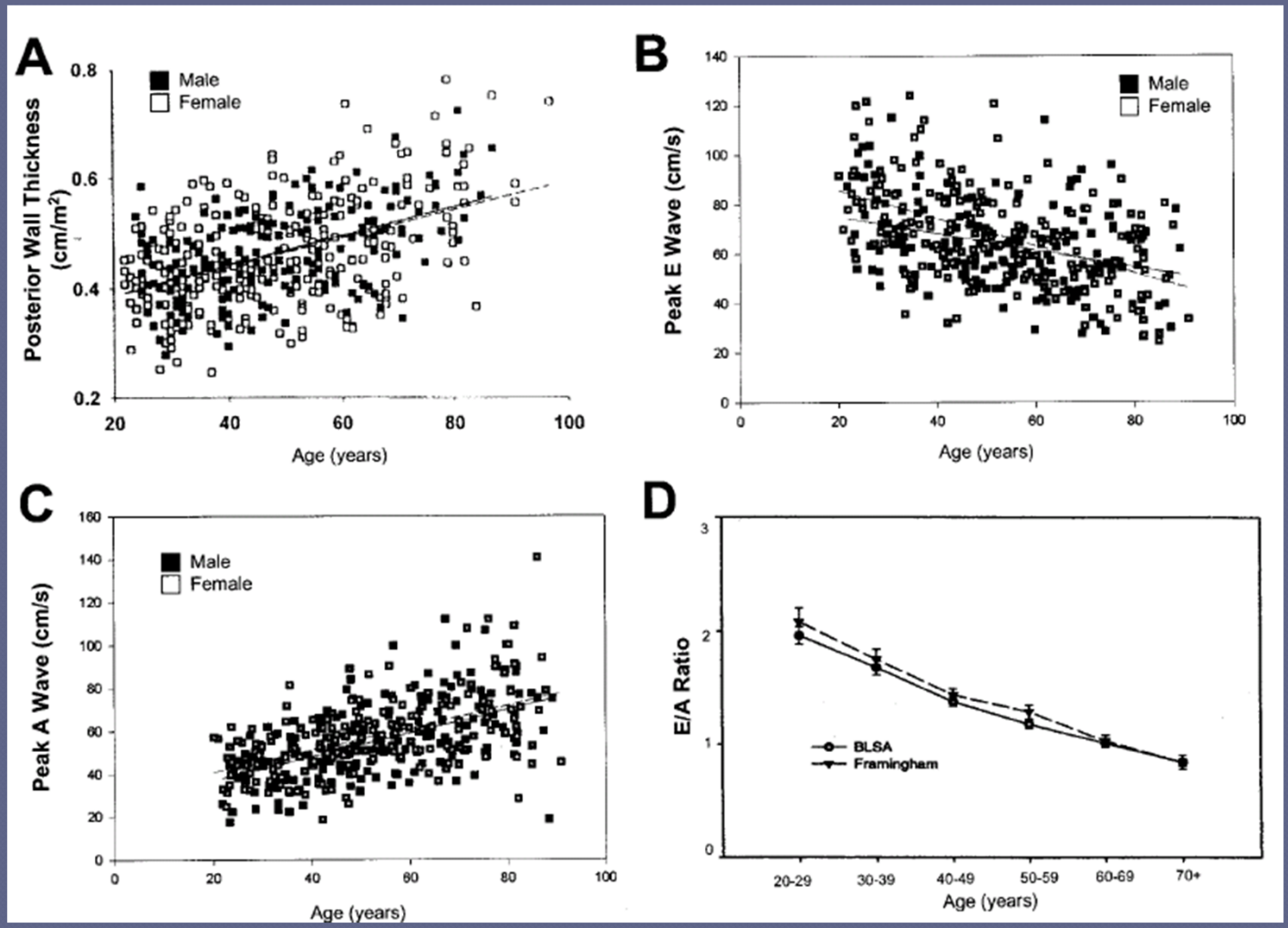
- Aging is associated with HF, Stroke and HT
- Vascular change with aging is similar to atherosclerosis and hypertensive change
- Aging is an independent factor for CVD

LVH, HF, and AF increase with Age



Framingham Heart Study

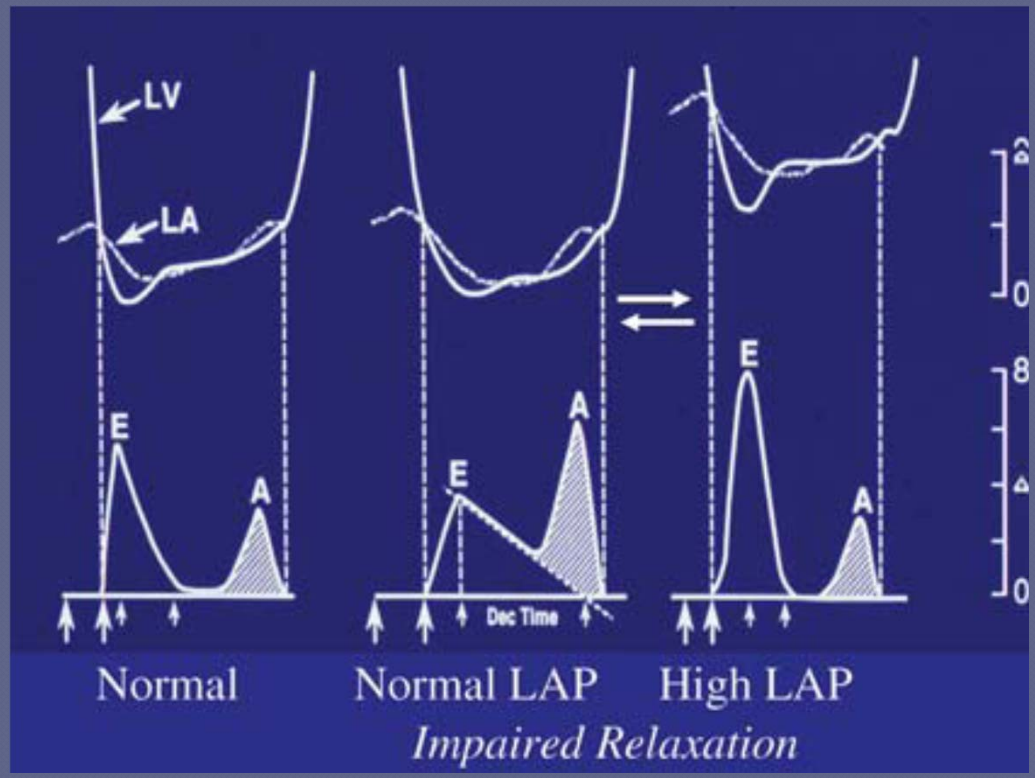
E/A decline with aging



Baltimore Longitudinal Study on Aging (BLSA)

Progression of Diastolic Dysfunction

1. Normal
2. Abnormal relaxation
3. Pseudonormalization
4. Restrictive pattern



Change in LV with aging

- leftventricular (LV) wall thickening:
  myocyte ↑ & collagen ↑
- LV early diastolic filling rate ↓ :
  fibrous change, Ca2+
- Change in EDV from rest to exercise significantly increases with age.

Aging of Cardiomyocytes

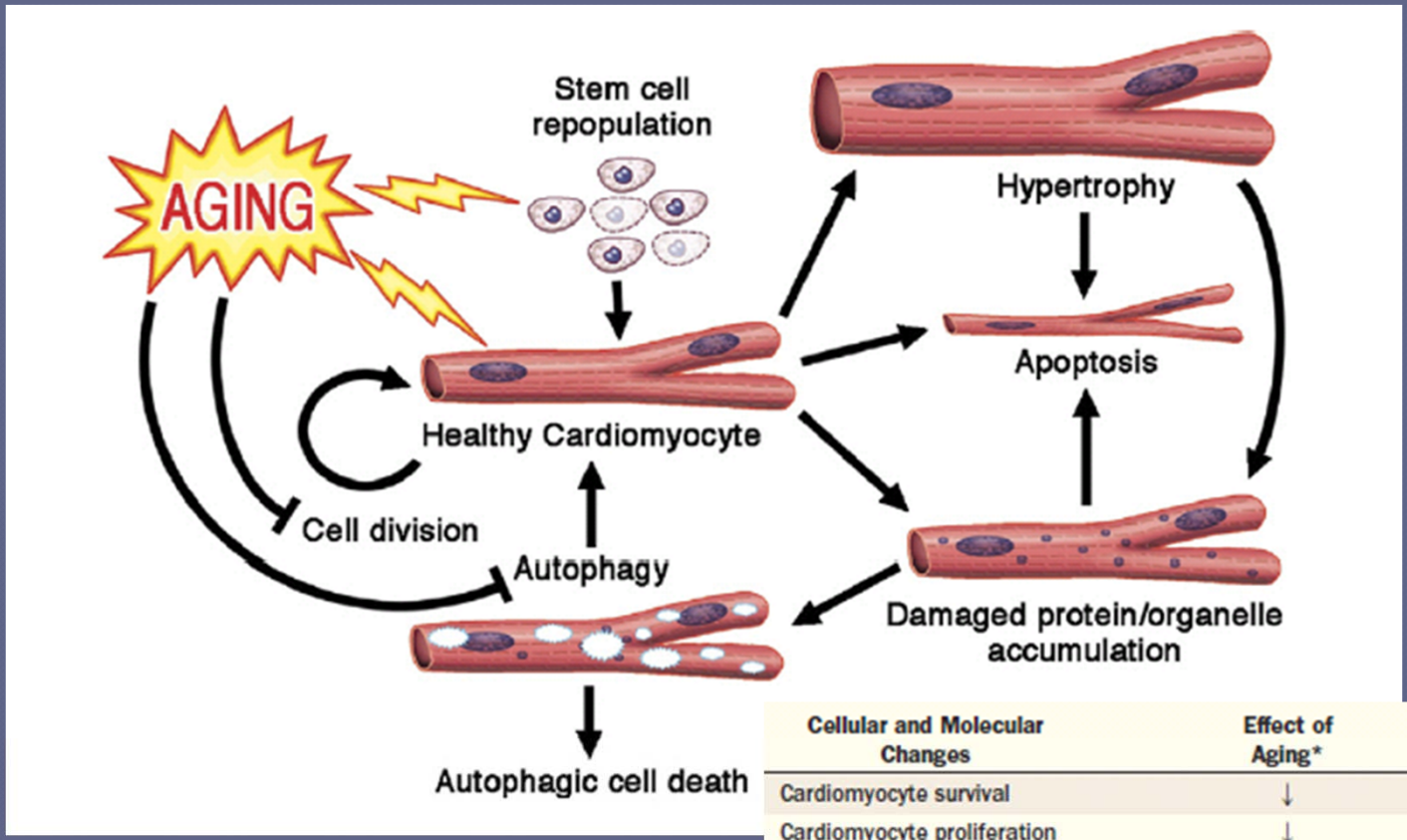
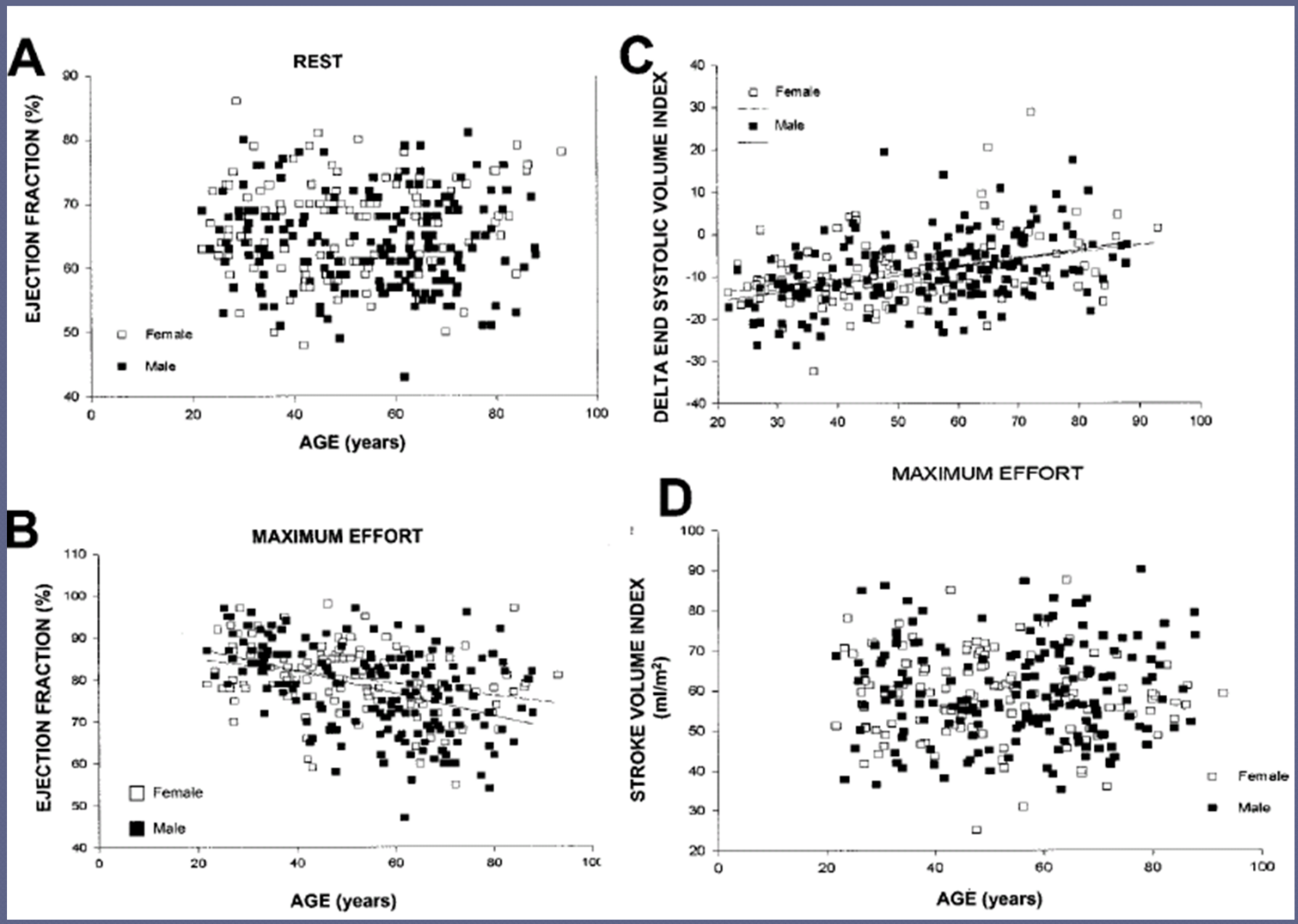


Figure illustration by Craig Skaggs

Cellular and Molecular Changes	Effect of Aging*	Clinical Effects at Baseline
Cardiomyocyte survival	↓	Impaired systolic function
Cardiomyocyte proliferation	↓	Impaired systolic function
Cardiac stem cell number	↓	Impaired systolic function
Cardiomyocyte diameter	↑	LV hypertrophy
Myocardial fibrosis	↑	Diastolic dysfunction
Dysfunctional fibroblasts	↑	Diastolic dysfunction

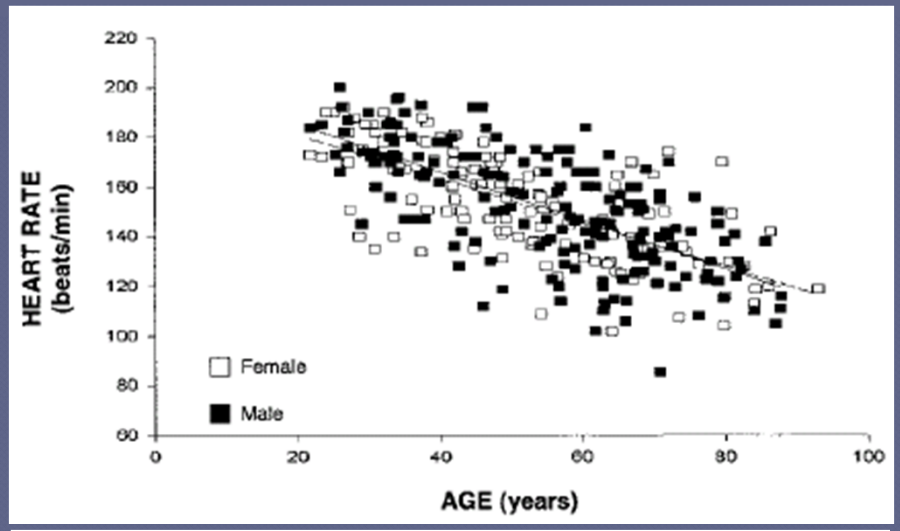
*Downward-pointing arrow (↓) indicates a decrease in effects; upward-pointing arrow (↑) indicates an increase.
LV = left ventricular; MI = myocardial infarction.

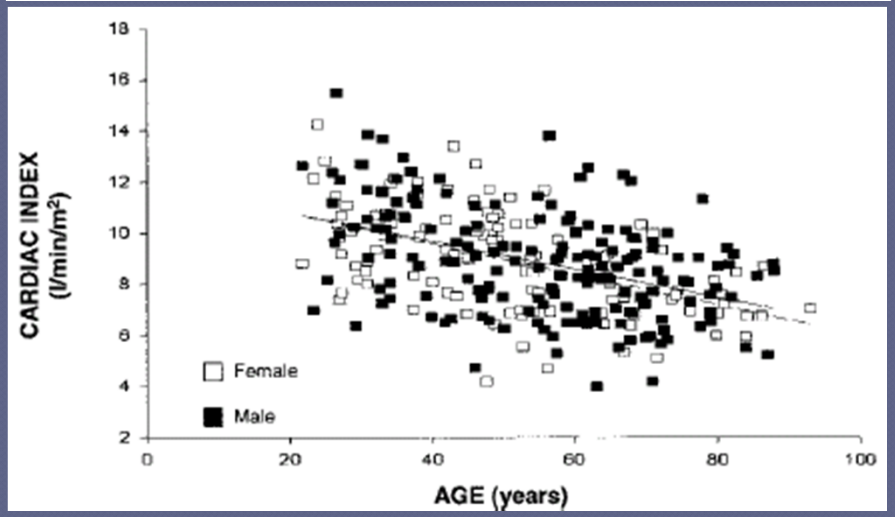
LV systolic function with aging

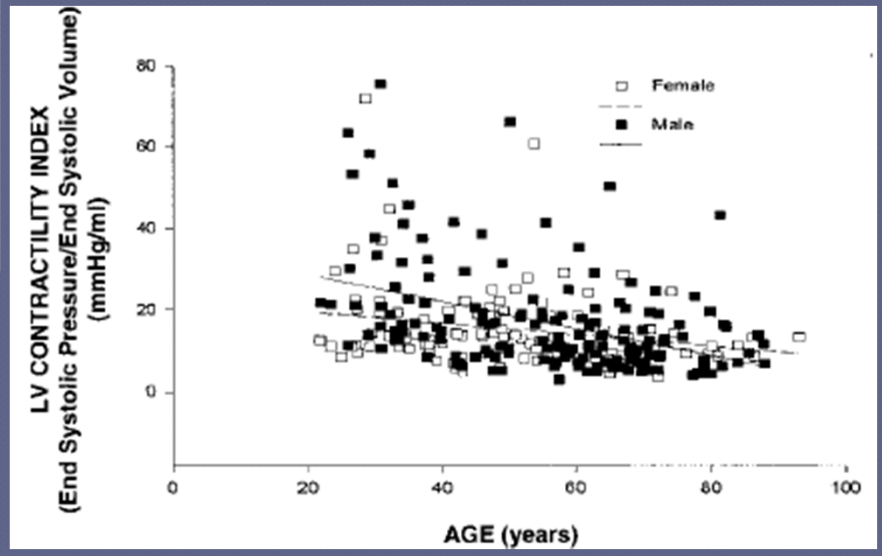


BLSA

HR, CO and LV contractility with aging



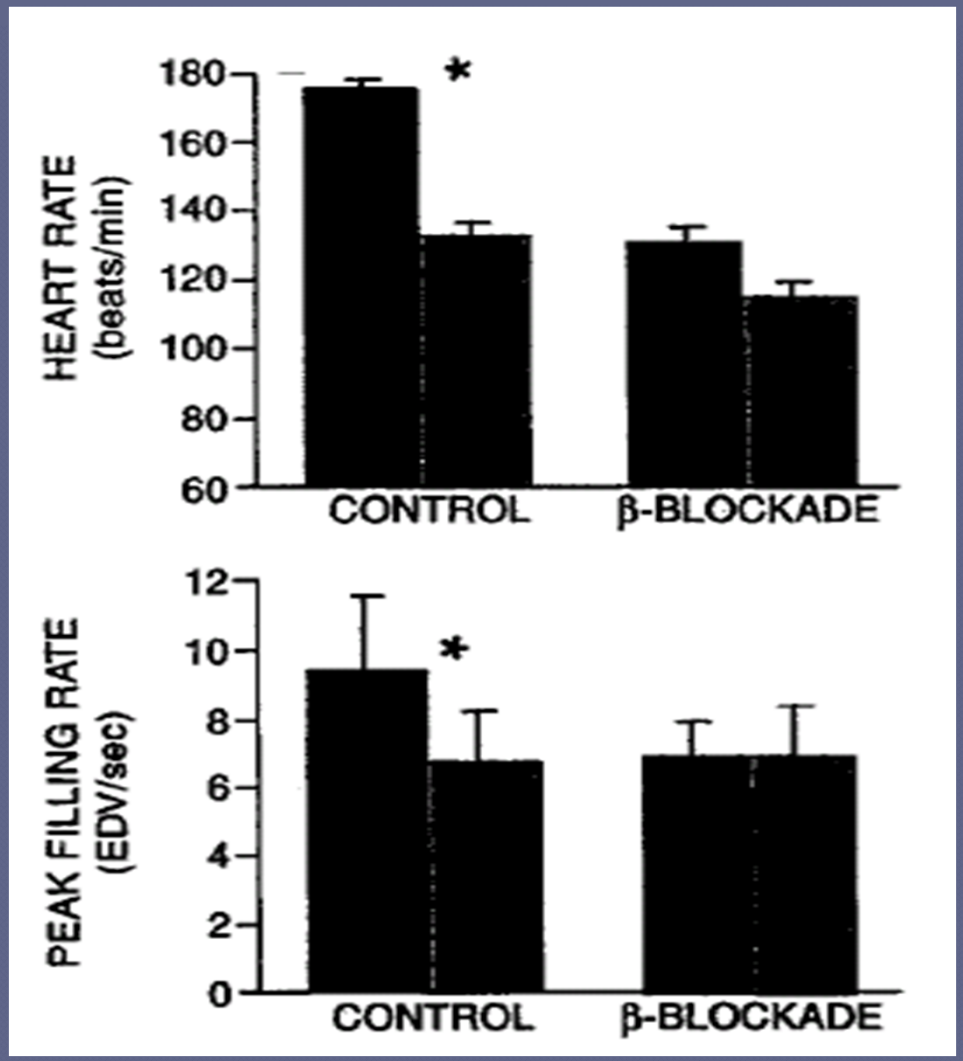




Deficient Cardiovascular Regulation With Aging in Healthy Humans

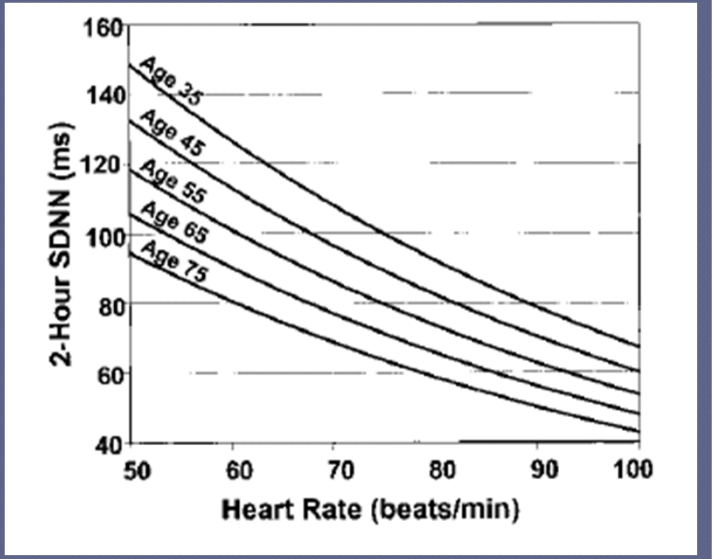
- Deficits in sympathetic modulation of Heart Rate and LV contractility
- Elaboration of catecholamines
- Impaired responses to -adrenergic receptor stimulation

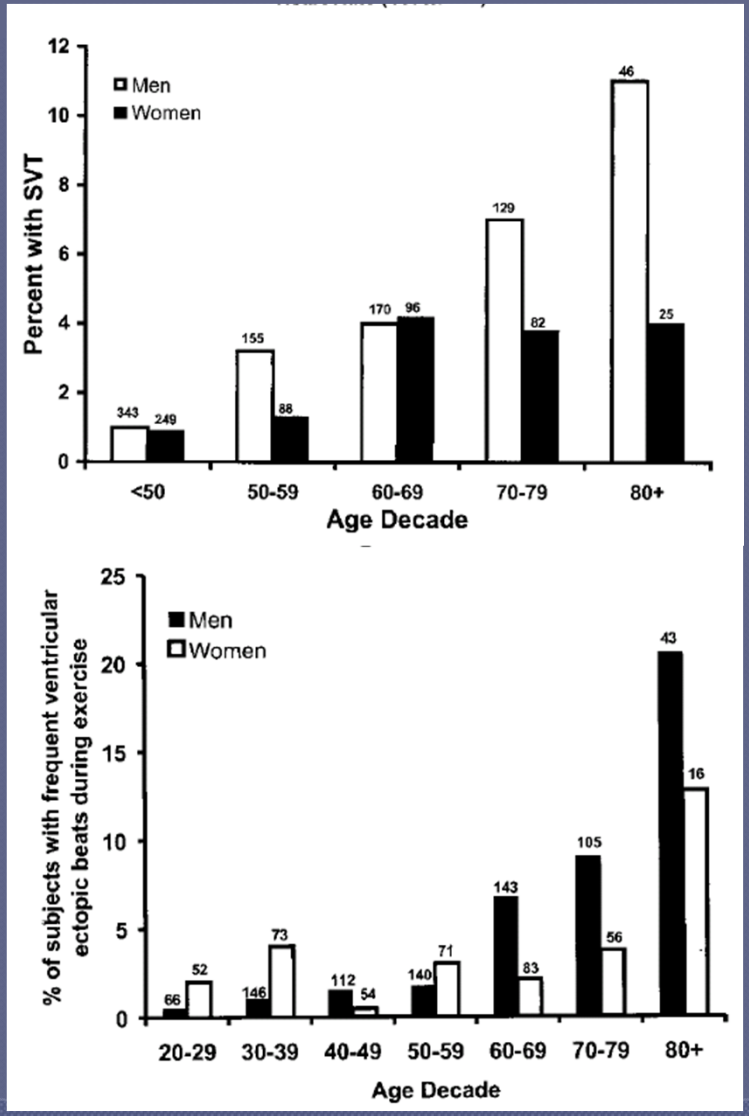
Difference of BB effect with exercise between young and old



First bars < 40 years;
Second bars > 60 years

HR variability and arrhythmia





Assessment of Myocardial Aging

- Echo:

  LVH (좌심실 심근비대)

  좌심실 확장기능평가: Doppler

  LVEF, ESVI/EDVI, LV elastance (ESP/ESV)

- Holter: HR variability, Premature Beats or AF
- Cardiac CT and cardiac MRI

LVH by M-mode

The calculation of LVM
is based on a mathematical formula
(prolate ellipsoid LV, long/short axis length =2)

LV Mass (g) =

$$0.8 * \left(\frac{1.04*[(LVIDd + PWTd + IVSTd)^3 - (LVIDd)^3]}{}\right) + 0.6$$

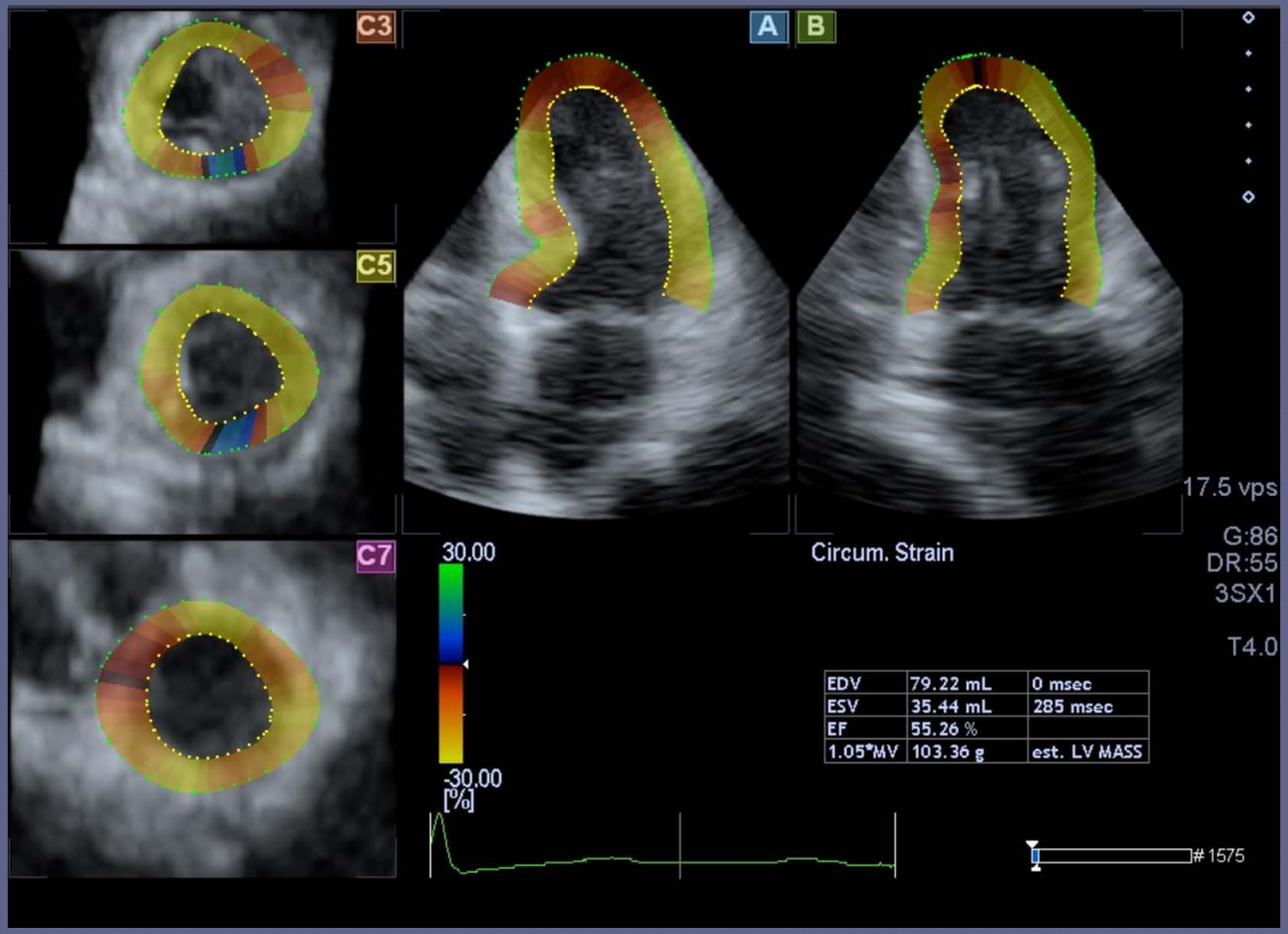
as modified by Devereux et al. using the
American Society of Echocardiography (ASE)

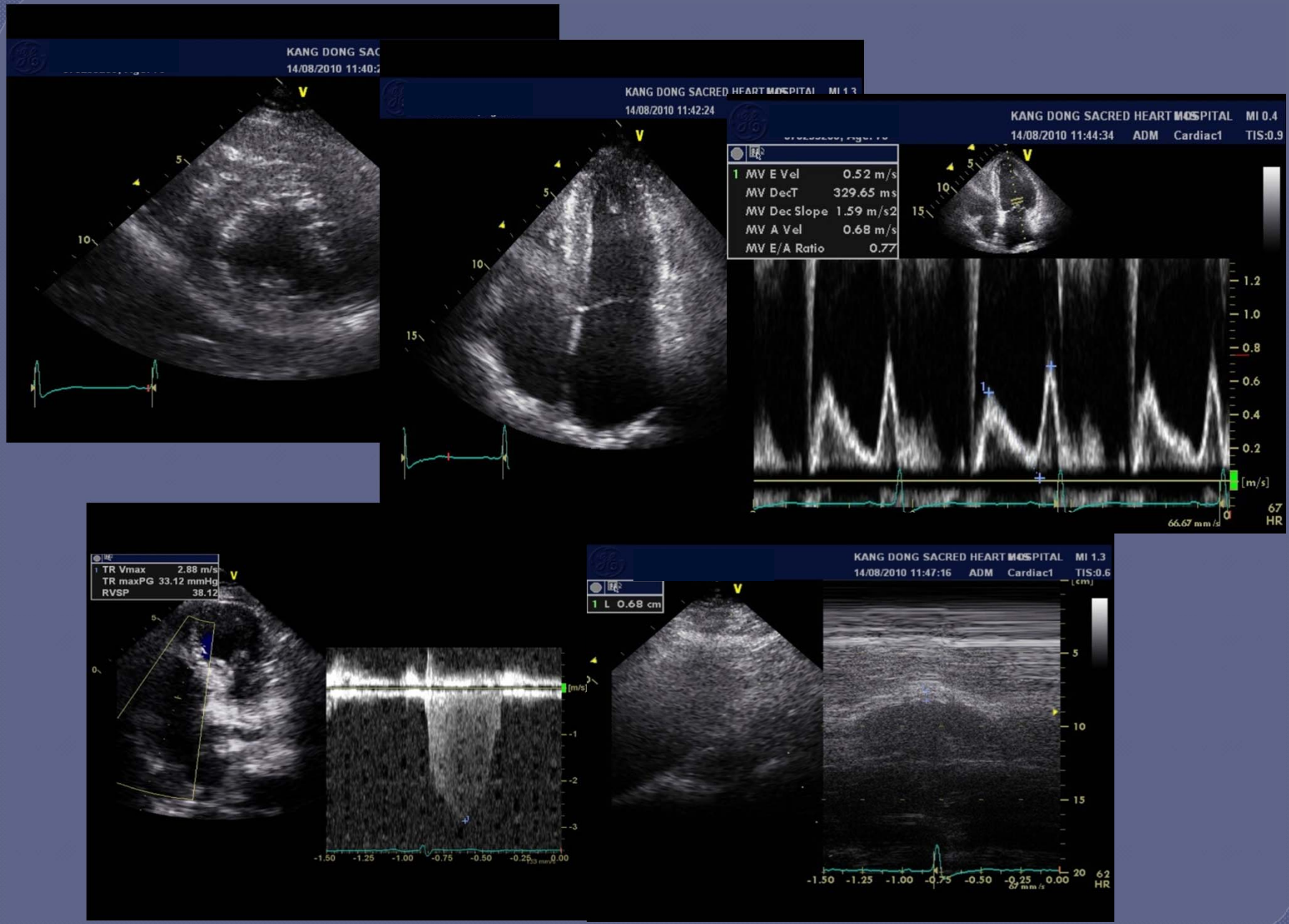
Table 1 Partition values for electrocardiogram (ECG) criteria of left ventricular hypertrophy (LVH), upper limit of normal for left ventricular mass (LVM) indexed to body surface area (BSA) for M-mode and two-dimensional echocardiography as well as cardiac magnetic resonance imaging (MRI)

	Male	Female
ECG		
Sokolow–Lyon (LIFE study)	$\geq$ 38 mm	$\geq$ 38 mm
Cornell	$\geq$ 28 mm	$\geq$ 20 mm
Cornell product	$\geq$ 2440 mm/ms	$\geq$ 2440 mm/ms
Sokolow–Lyon product	$\geq$ 4000 mm/ms	$\geq$ 3000 mm/ms
Echocardiography		
M-mode LVM indexed BSA	$\geq$ 125 g/m^2	$\geq$ 110 g/m^2
2-D echo LVM indexed BSA	$\geq$ 102 g/m^2	$\geq$ 88 g/m^2
Cardiac MRI		
TGE LVM indexed BSA	$\geq$ 96 g/m^2	$\geq$ 77 g/m^2
SSFP indexed BSA	$\geq$ 83 g/m^2	$\geq$ 67 g/m^2

2-D, two-dimensional; TGE, turbo gradient echo; SSFP, steady-state free precession.

LV mass measurement by 3D echo

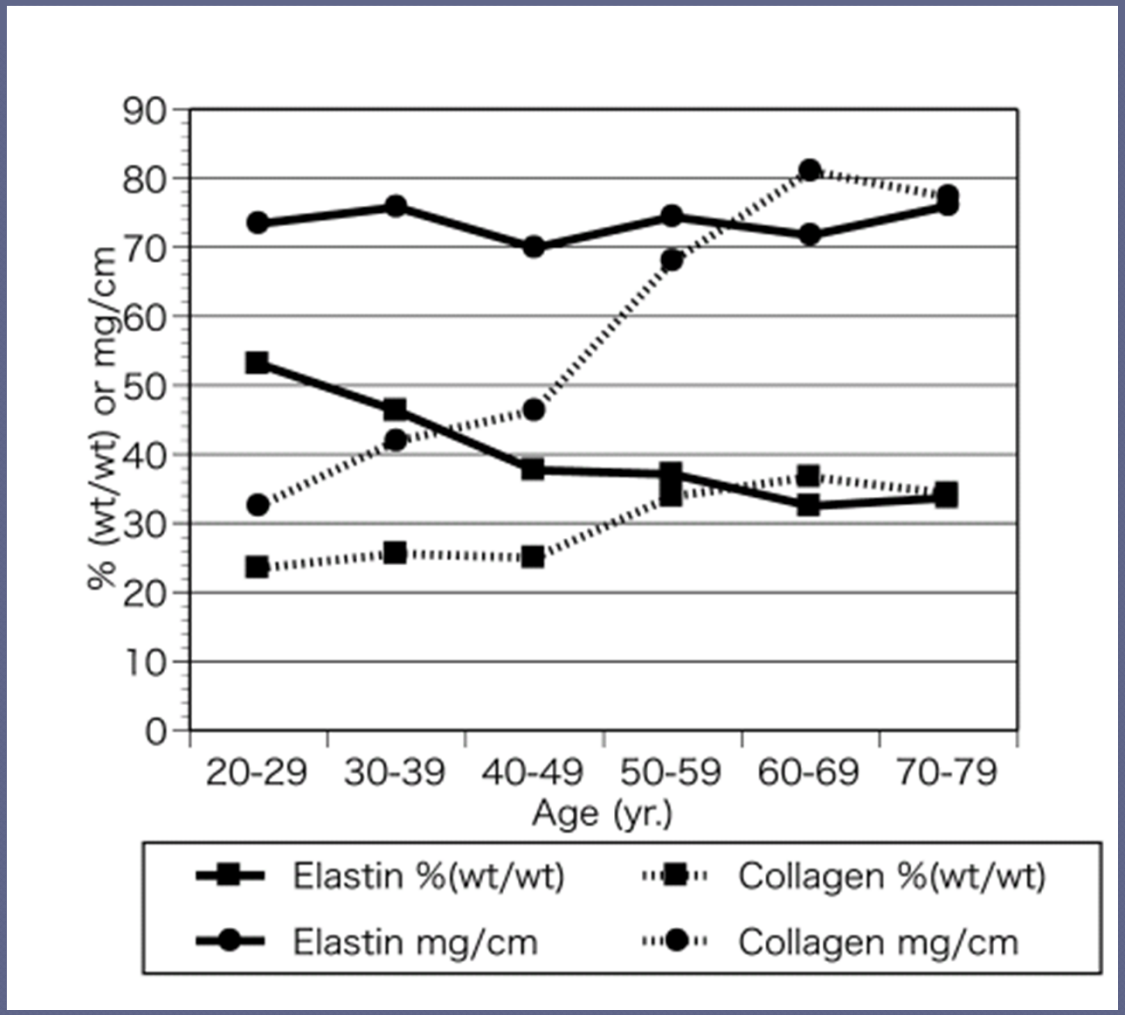



KANG DONG SACRED HEART HOSPITAL
14/08/2010 11:42:24
KANG DONG SACRED HEART HOSPITAL MI 0.4
14/08/2010 11:44:34 ADM Cardiac1 TIS:0.9
1 MV E Vel 0.52 m/s
MV DecT 329.65 ms
MV Dec Slope 1.59 m/s2
MV A Vel 0.68 m/s
MV E/A Ratio 0.77
[m/s]
HR
TR Vmax 2.88 m/s
TR maxPG 33.12 mmHg
RVSP 38.12
KANG DONG SACRED HEART HOSPITAL MI 1.3
14/08/2010 11:47:16 ADM Cardiac1 TIS:0.6
1 L 0.68 cm
[cm]
HR

Causes of arterial aging

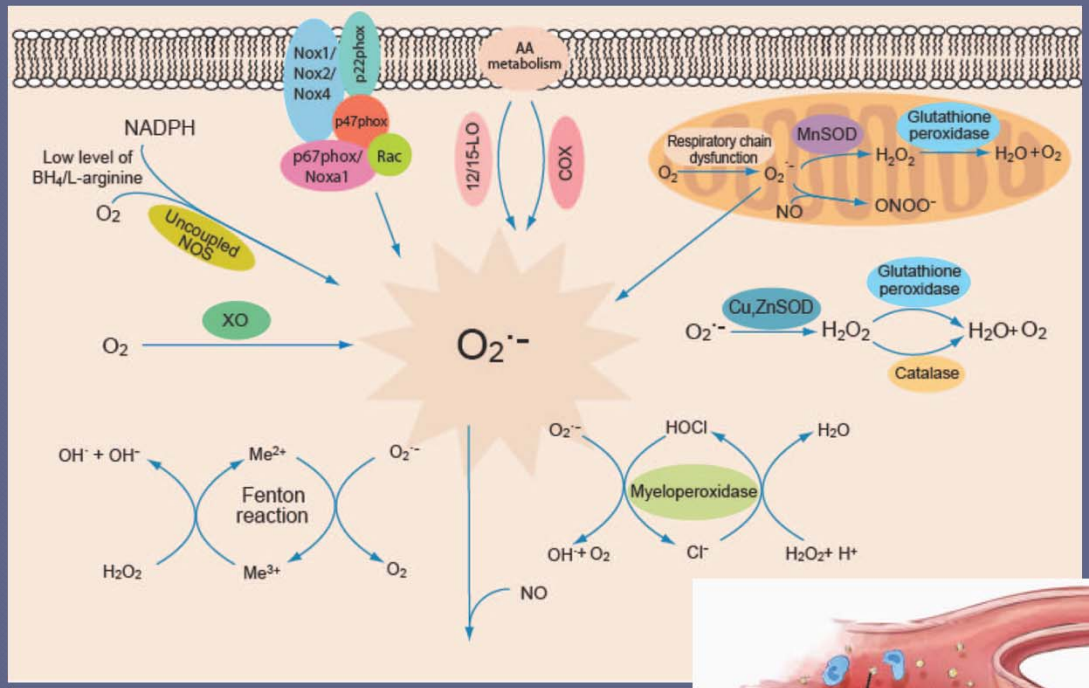
- **Endothelial cells:** Endothelial dysfunction
  ↑ NADPH oxidase
- **Intima:** ↑ Atheroma, Macrophages,
  ↑ Smooth muscle cells
- **Media & Adventitia:** Matrix remodeling:
  ↓ Elastin, ↑ Collagen, ↑ MMPs, ↑ VSMC, ↑ ICAM
- **Deposition:** AGEs, Calcium
- **Extrinsic Influences:** Hypertension,
- metabolic syndrome, Diabetes, etc

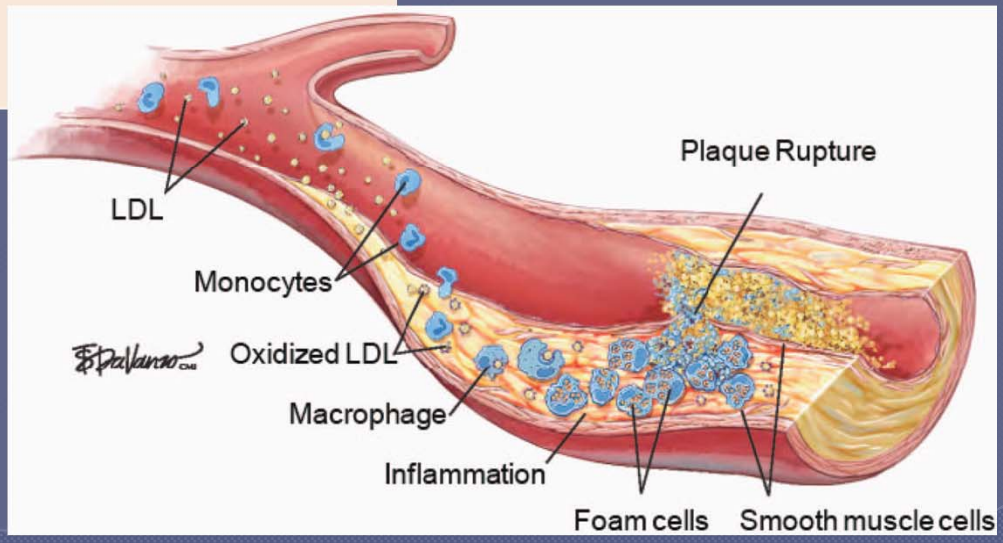
Elastin and Collagen in human upper thoracic aortic media with aging



Spina *et al.* *Arteriosclerosis 1983*

Sources of ROS in vascular cells

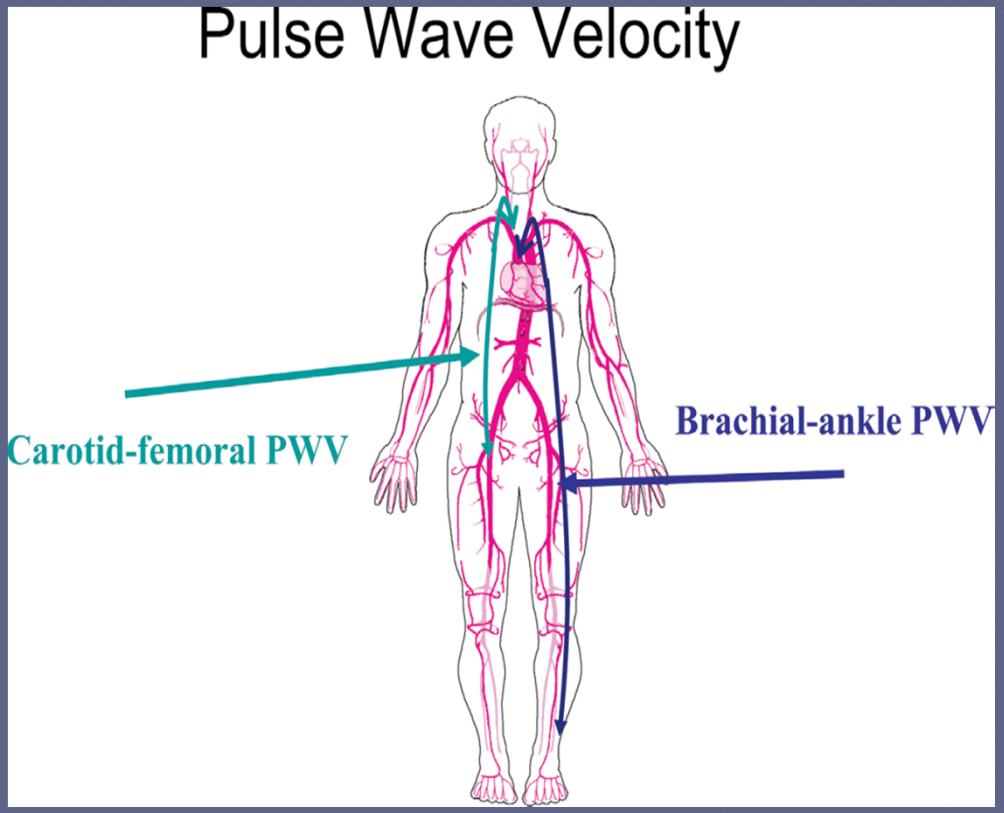


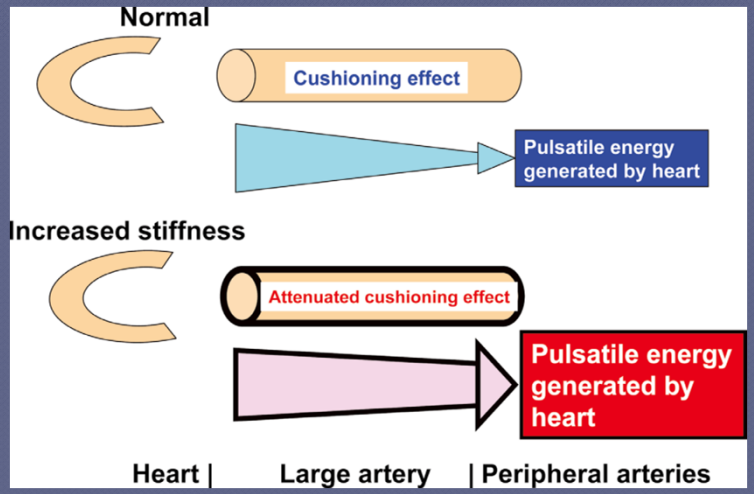


Assessment of Vascular aging, Preclinical status or Atherosclerosis

- Flow-mediated vasodilation (FMD)
- pulse wave velocity (PWV)
- carotid augmentation index (AIx)
- ankle brachial index (ABI)
- carotid IMT
- coronary artery calcification
- mitral annular calcification and AV sclerosis

PWV (pulse wave velocity):
stiffness of central artery

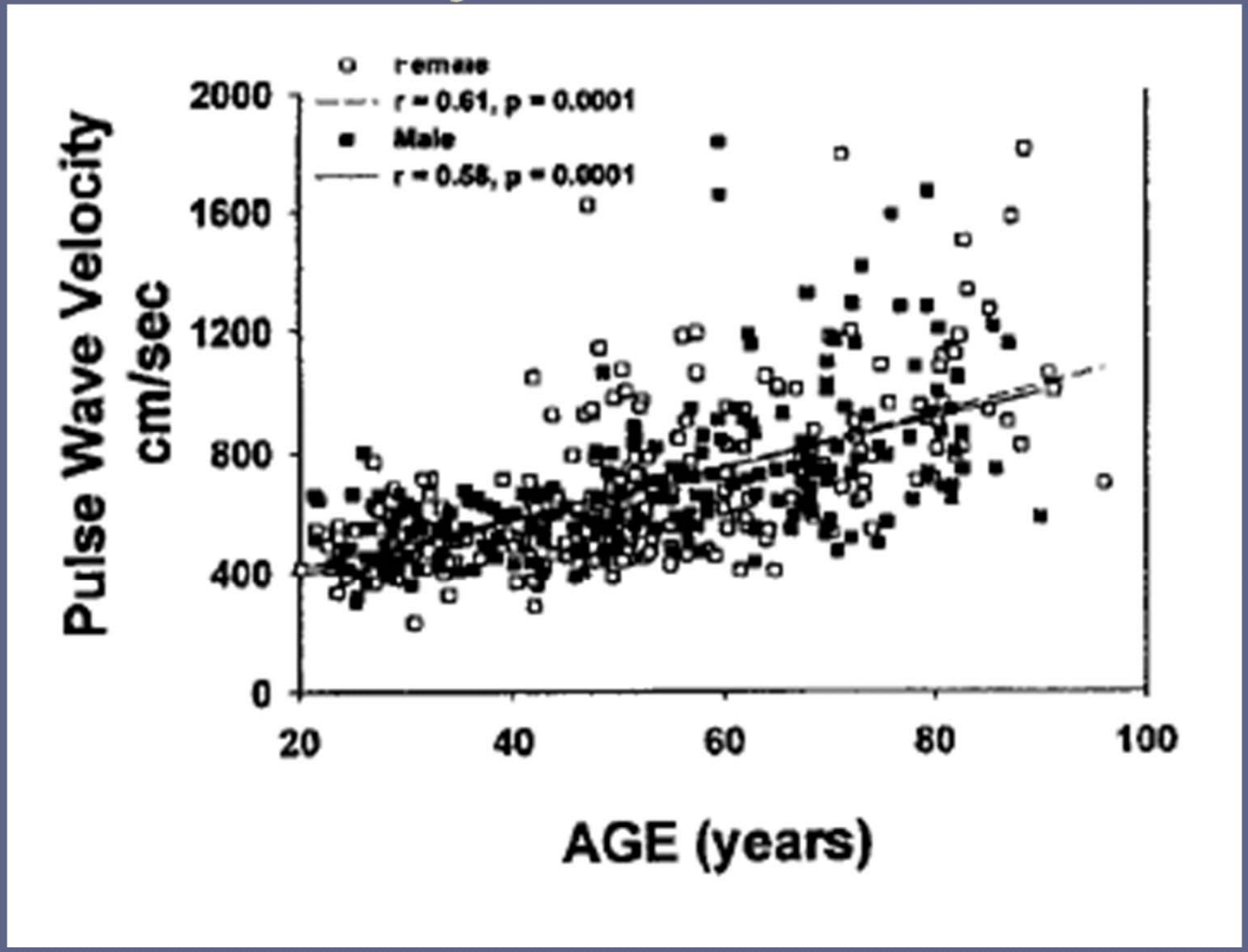




Carotid – femoral PWV:
- **the gold standard**
- **an independent predictor of cardiovascular mortality and morbidity in elderly subjects**

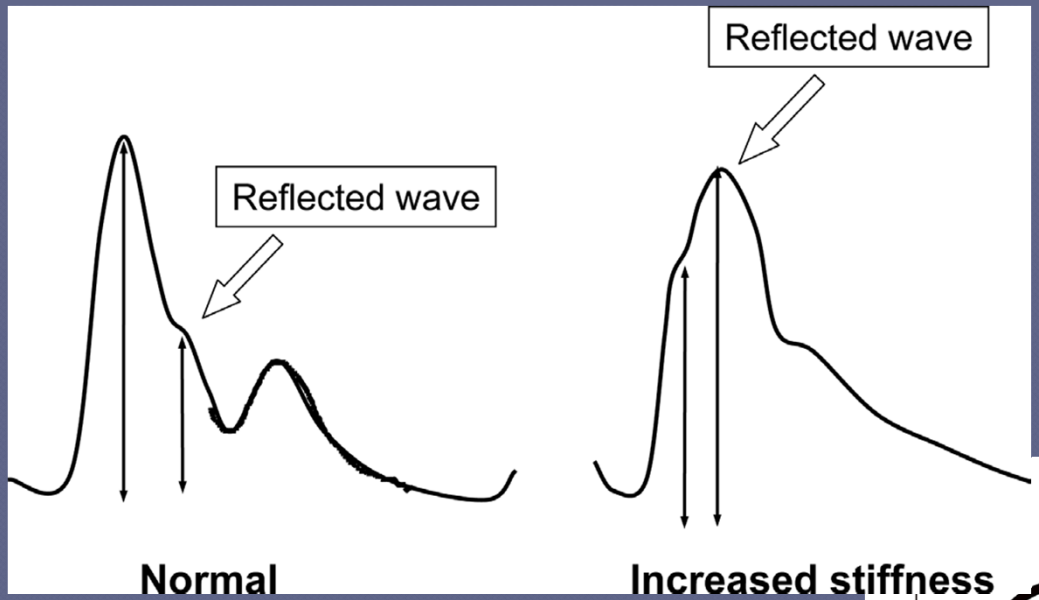
C-f PWV > 12 m/sec

Aortic pulse wave velocity in healthy BLSA volunteer subjects

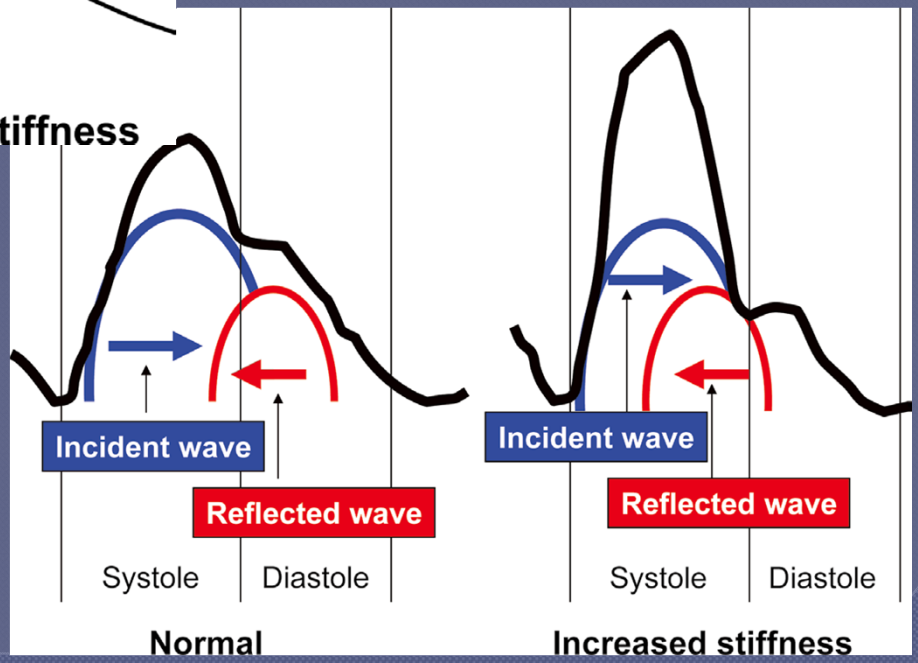


Circulation 1993;88:1456–1462

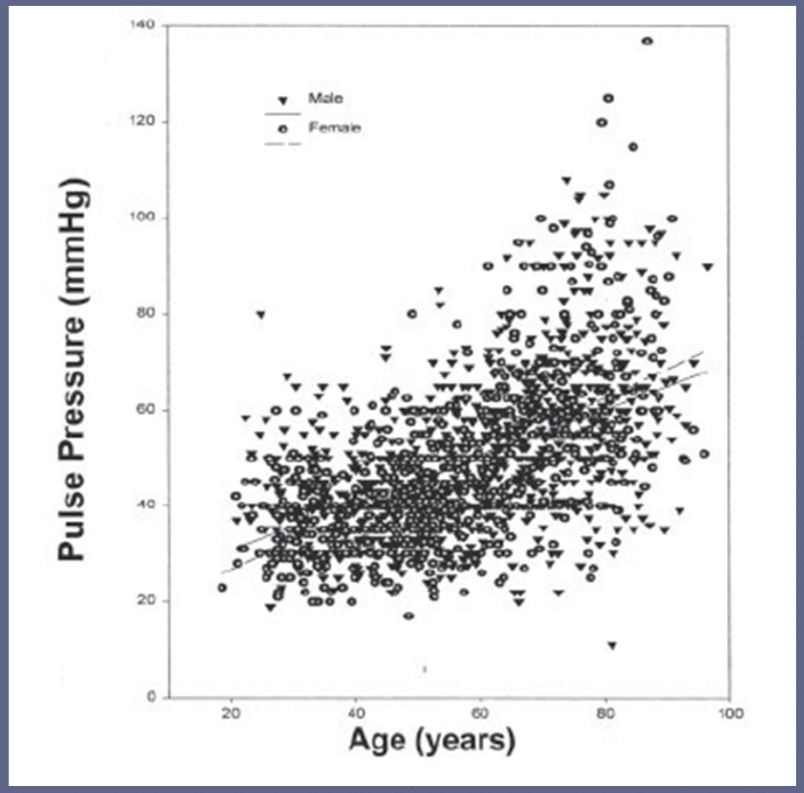
Reflected wave (augmentation)



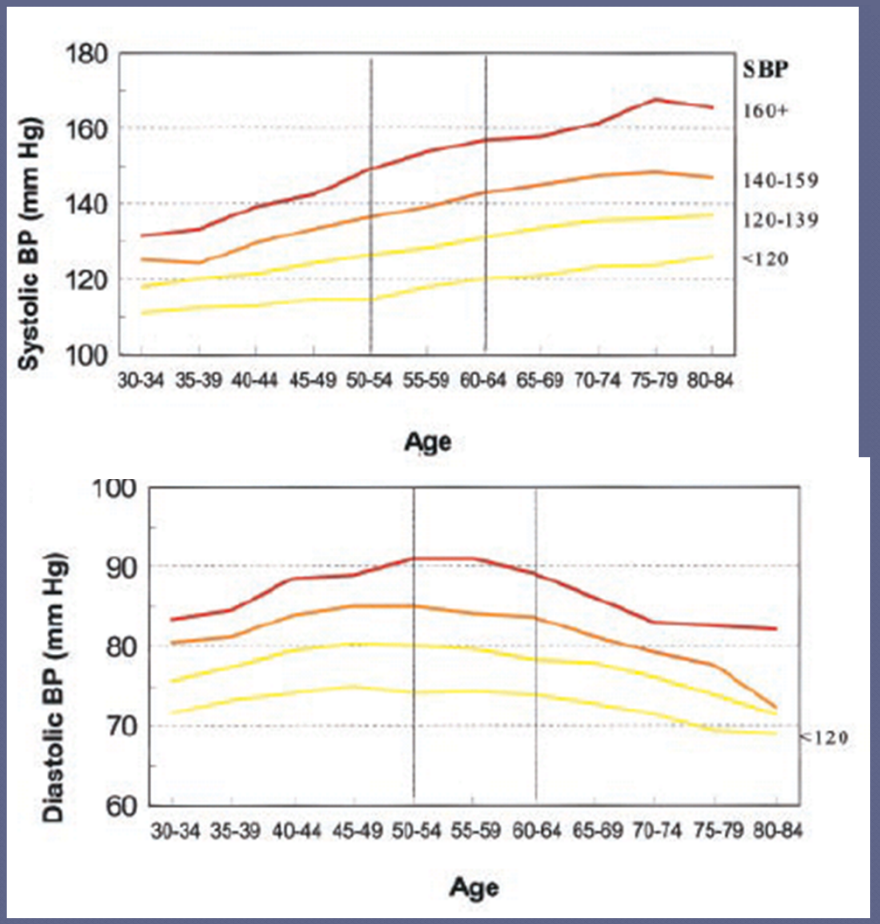
Augmentation Index
= AP/ SBP-DBP



PP (SBP-DBP) with aging

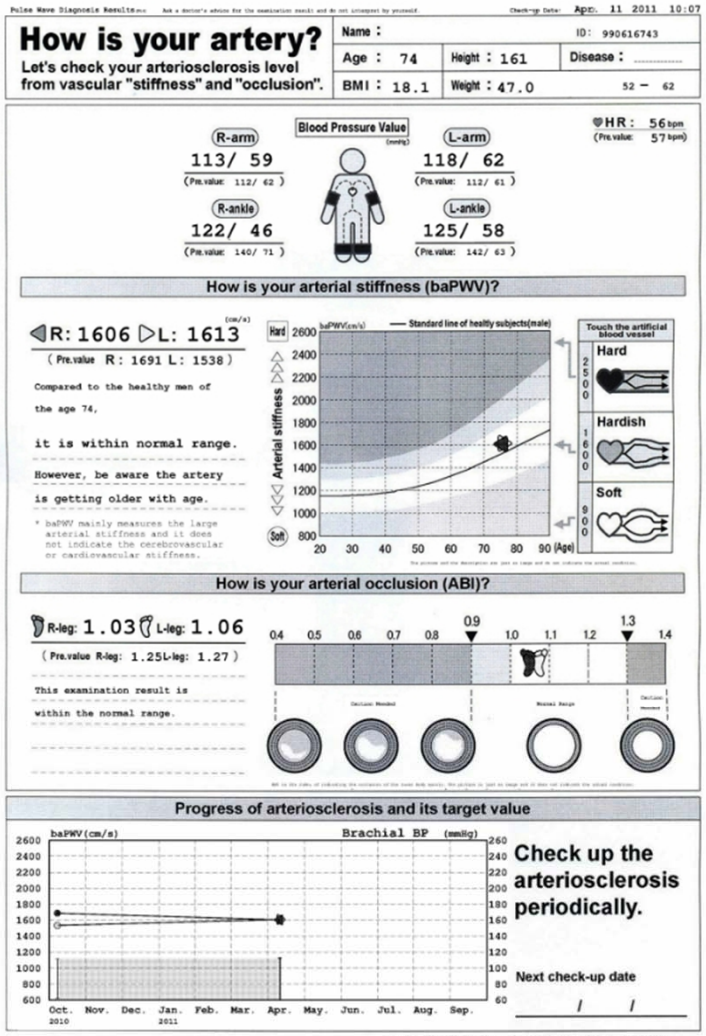


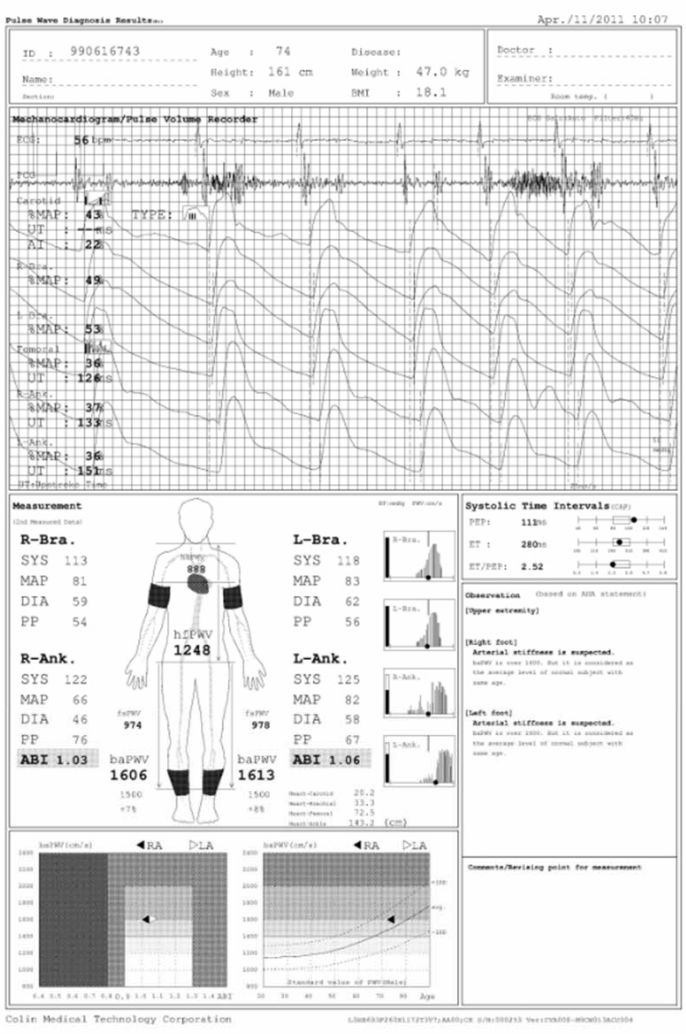
Pulse pressure in healthy (BLSA)



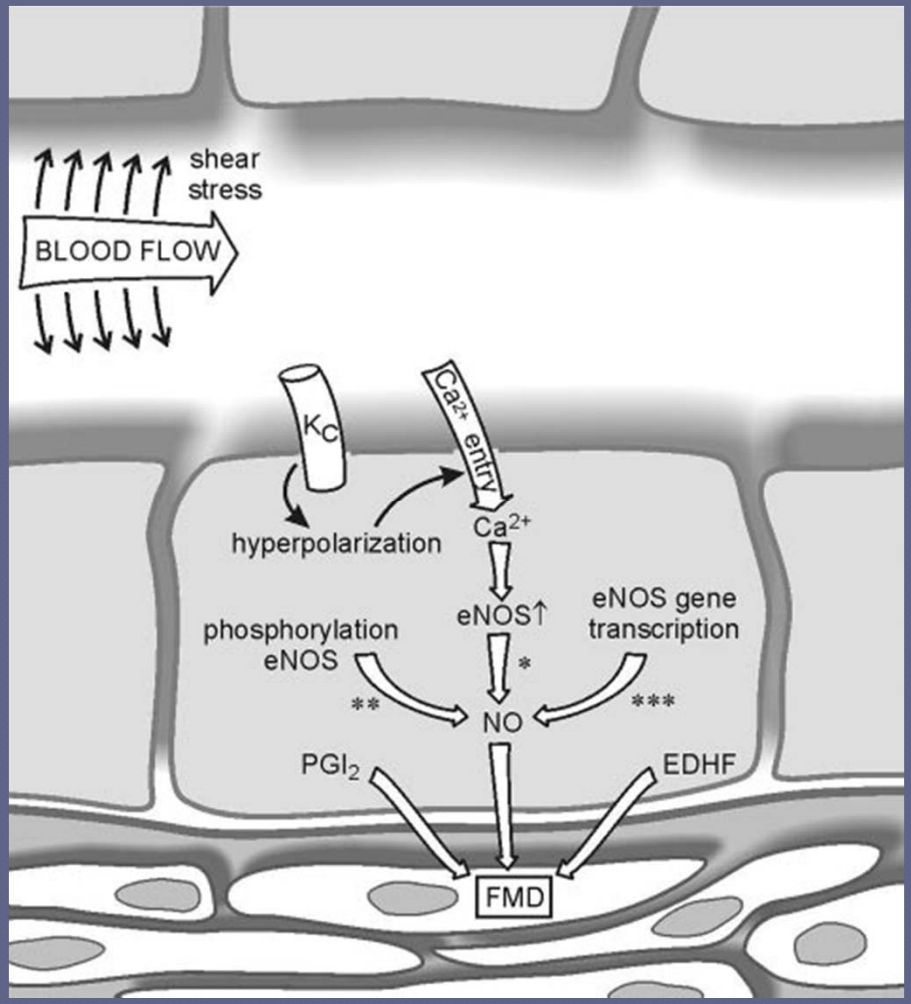
Framingham Heart Study

PWV, AI and ABI (Colin VP200)



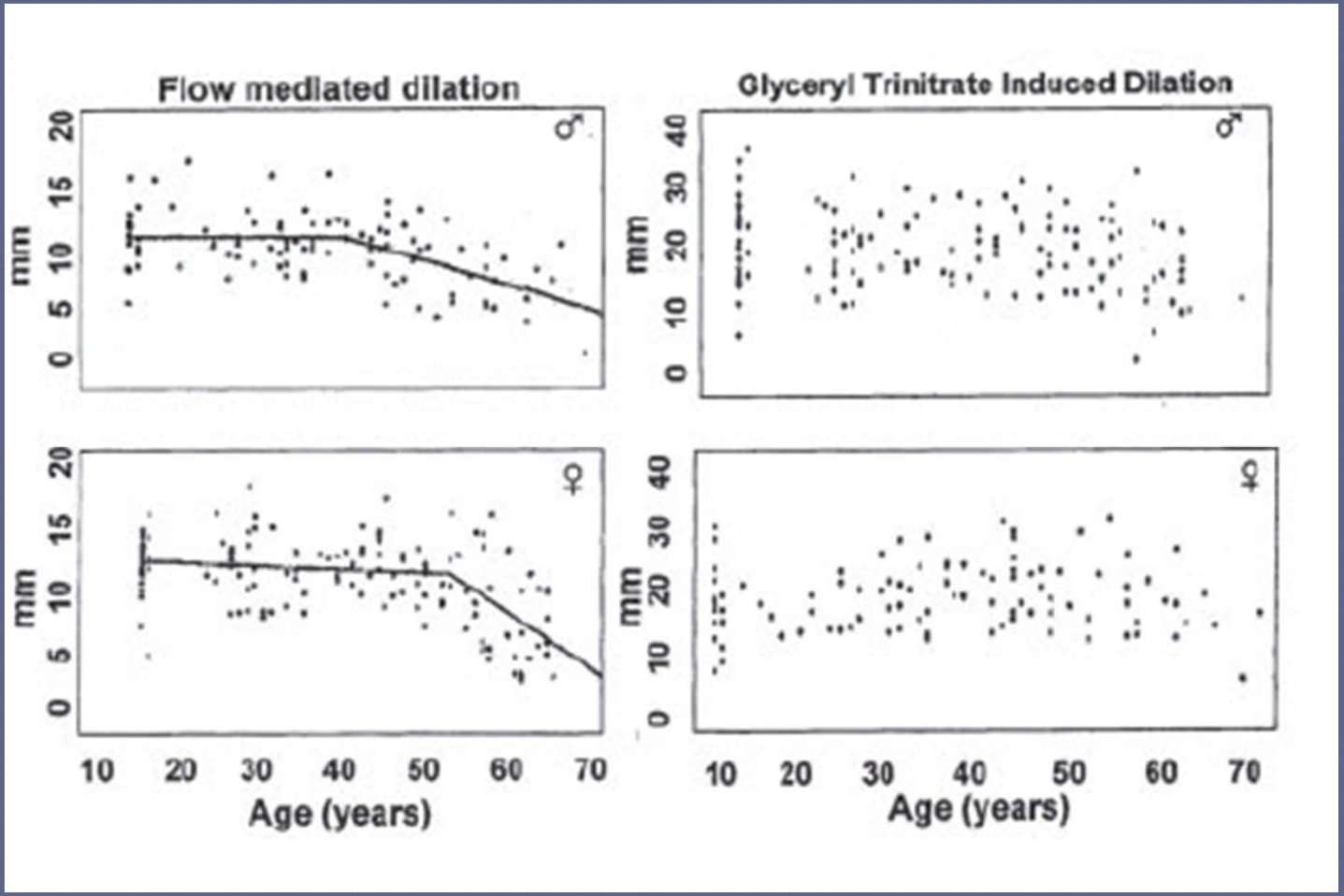


Flow mediated Vasodilation (FMD)

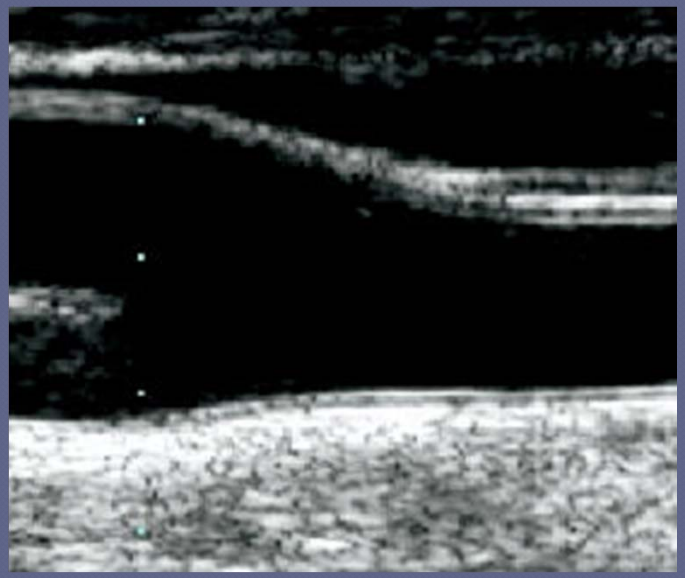


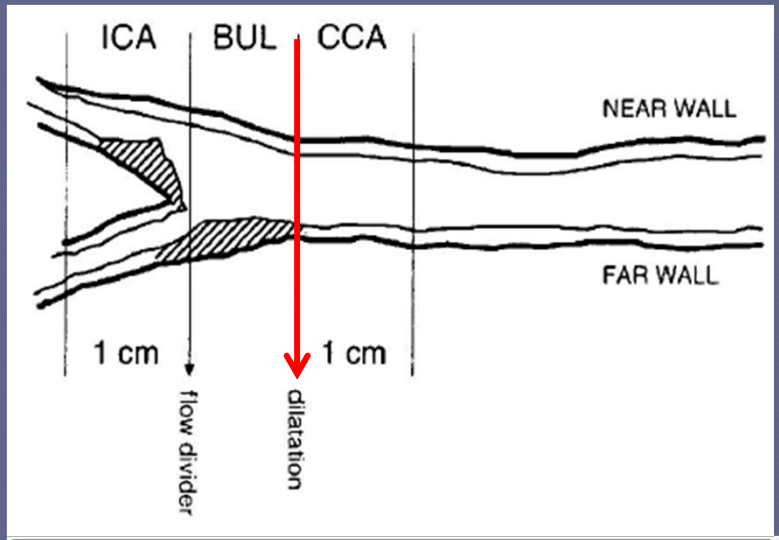
Impaired brachial-artery endothelial function independently predicts long-term cardiovascular events in patients with peripheral arterial disease. The findings suggest that noninvasive assessment of endothelial function using brachial-artery FMD may serve as a surrogate end point for cardiovascular risk. (J Am Coll Cardiol 2003;41:1769 –75)

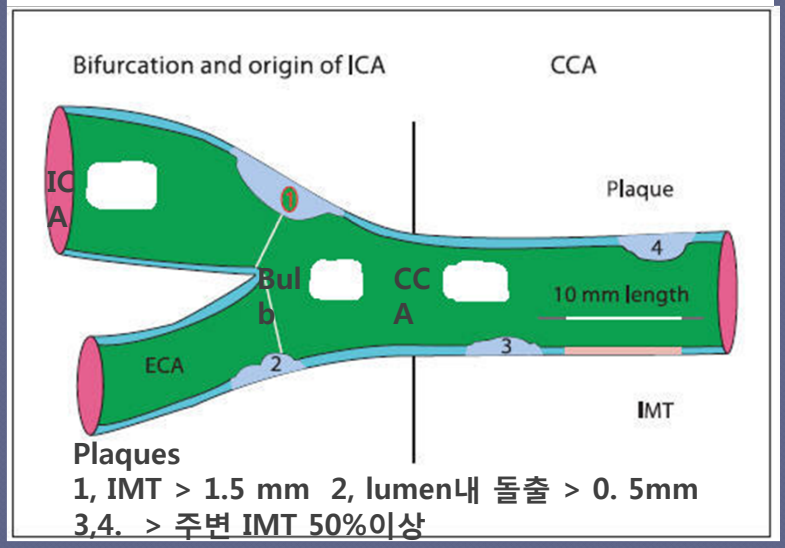
FMD (endothelial function) with age



Carotid IMT





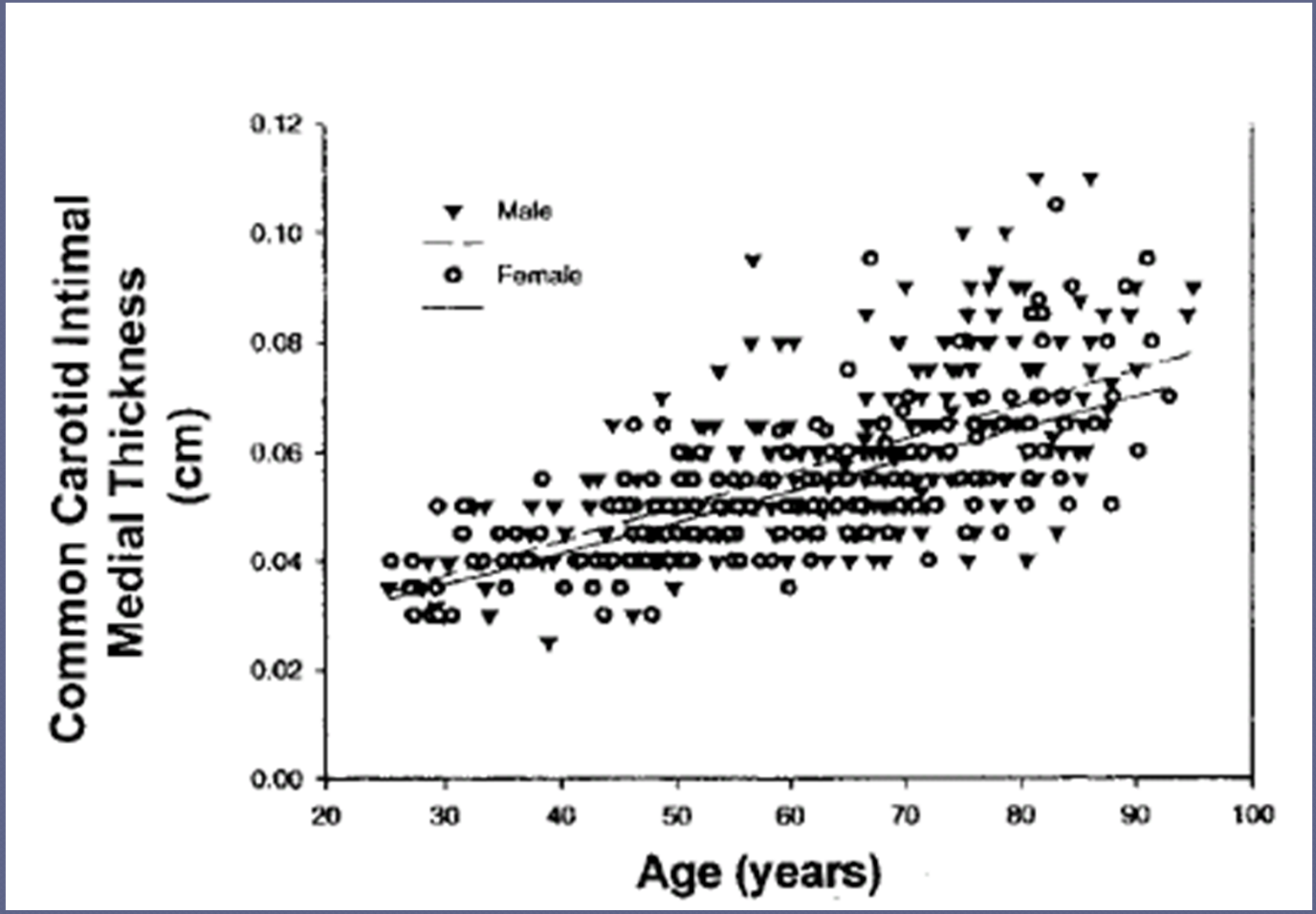


Plaques

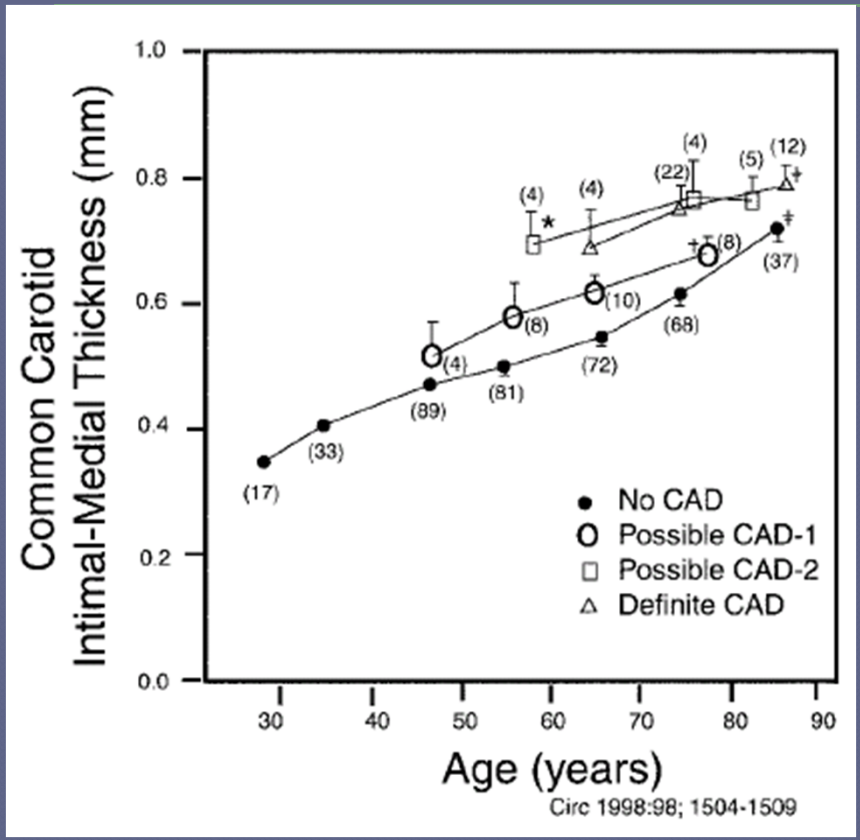
1, IMT > 1.5 mm 2, lumen내 돌출 > 0. 5mm

3,4. > 주변 IMT 50%이상

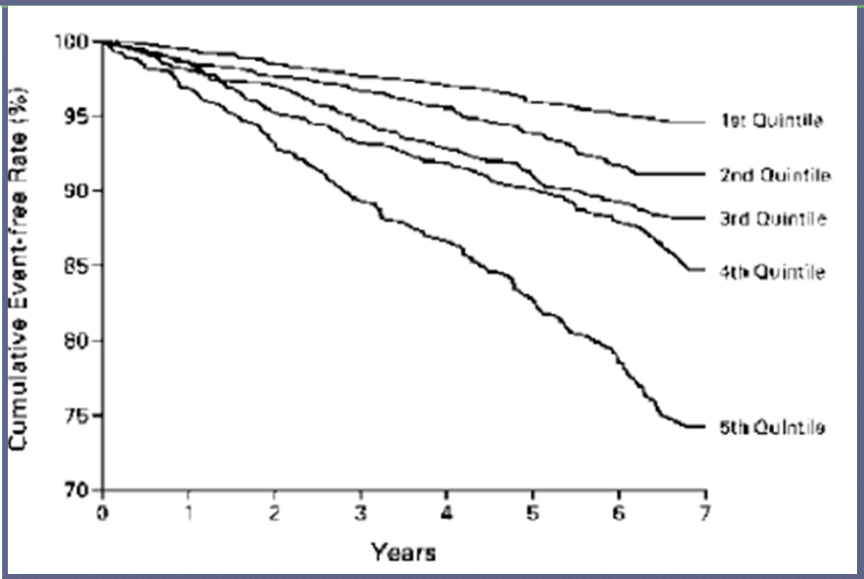
The common carotid IMT in healthy BLSA volunteers as a function of age



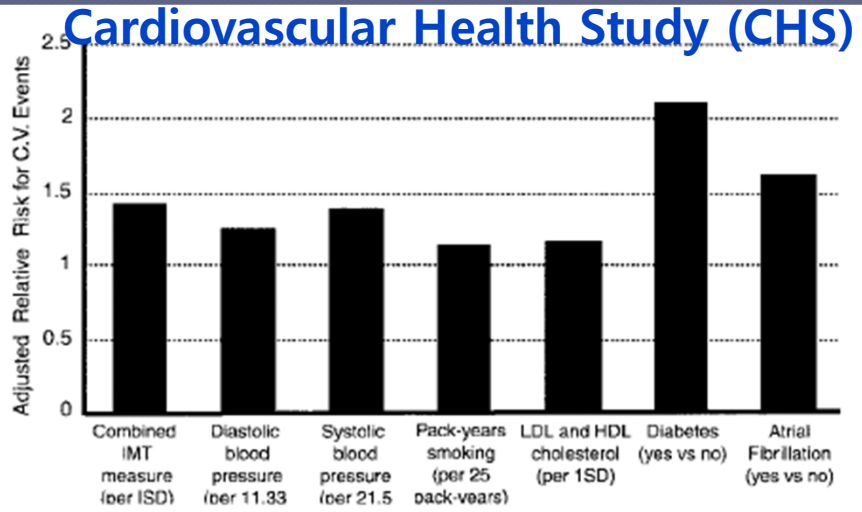
Carotid IMT as a risk factors or subclinical disease



Circulation 1998;98:1504- 1509.



Cardiovascular Health Study (CHS)



Traditional risk factors accelerate aging of vascular walls, especially at younger ages

Coronary artery calcium score

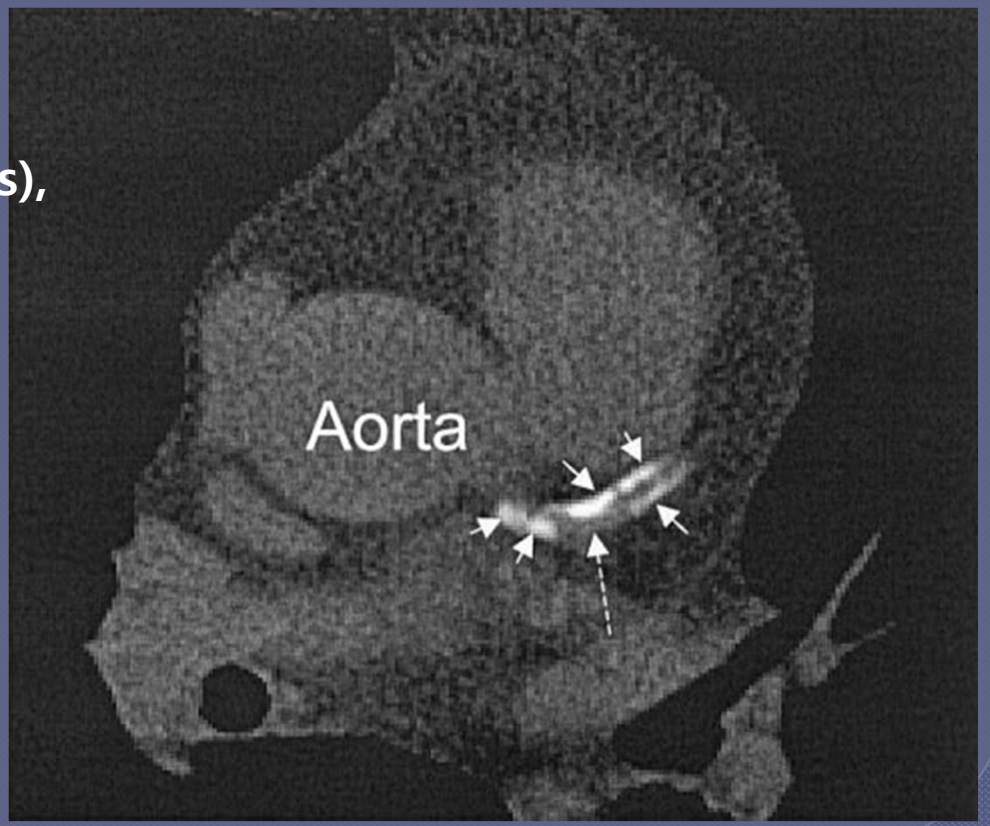
Agatston score:

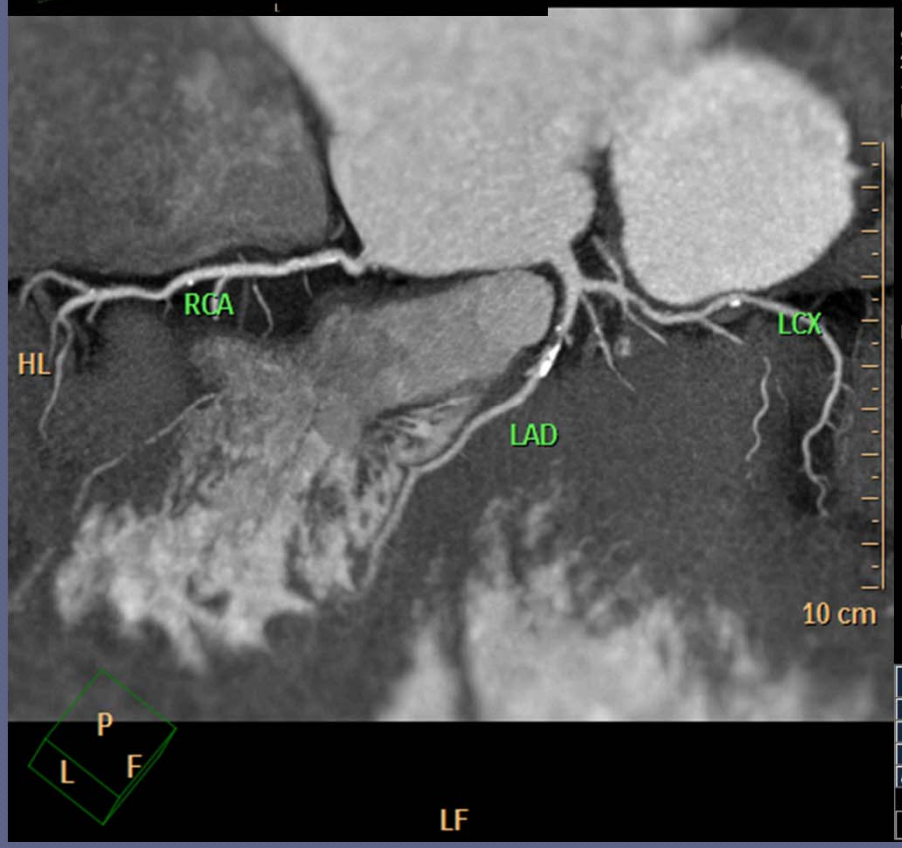
$$\sum (\text{pixel} \times \text{density} \times \text{slice thickness}/3)$$

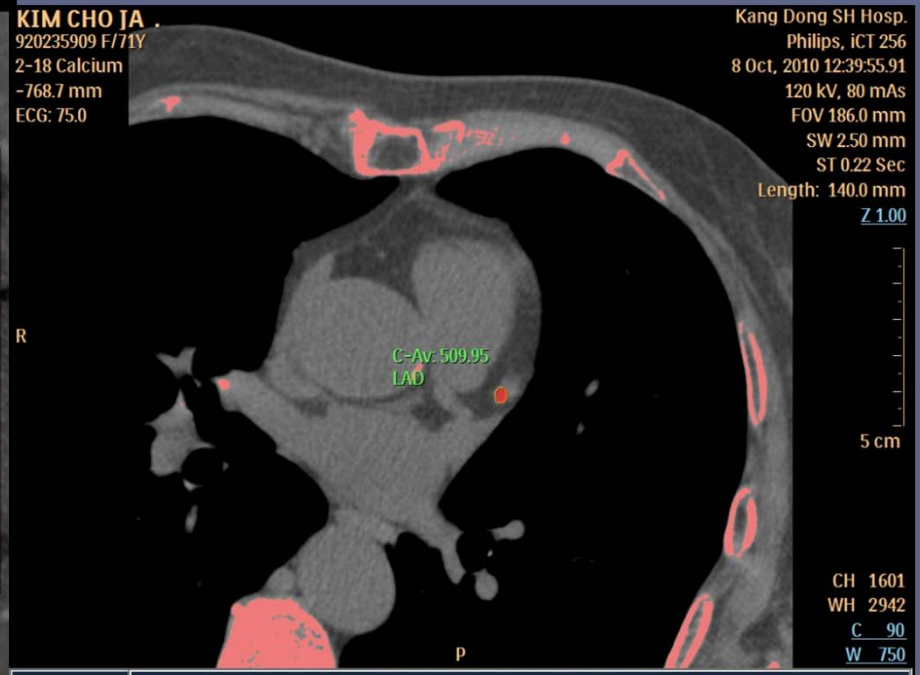
Density:

1 for 130-199 HU (Hounsfield units),
2 for 200-299 HU,
3 for 300-399 HU, and
4 for 400 HU and greater

The tomographic slices (3 mm):
50-60 slices



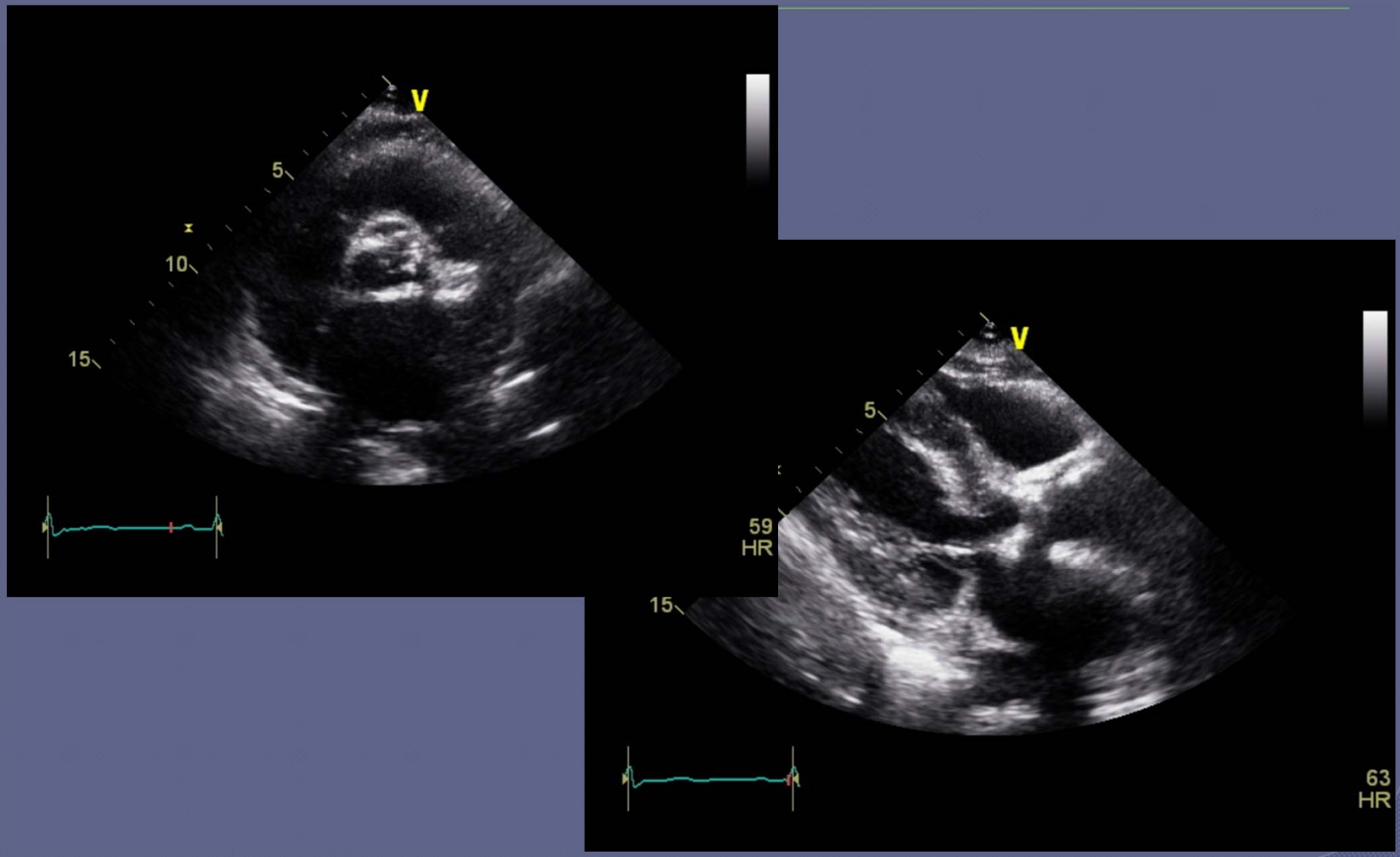




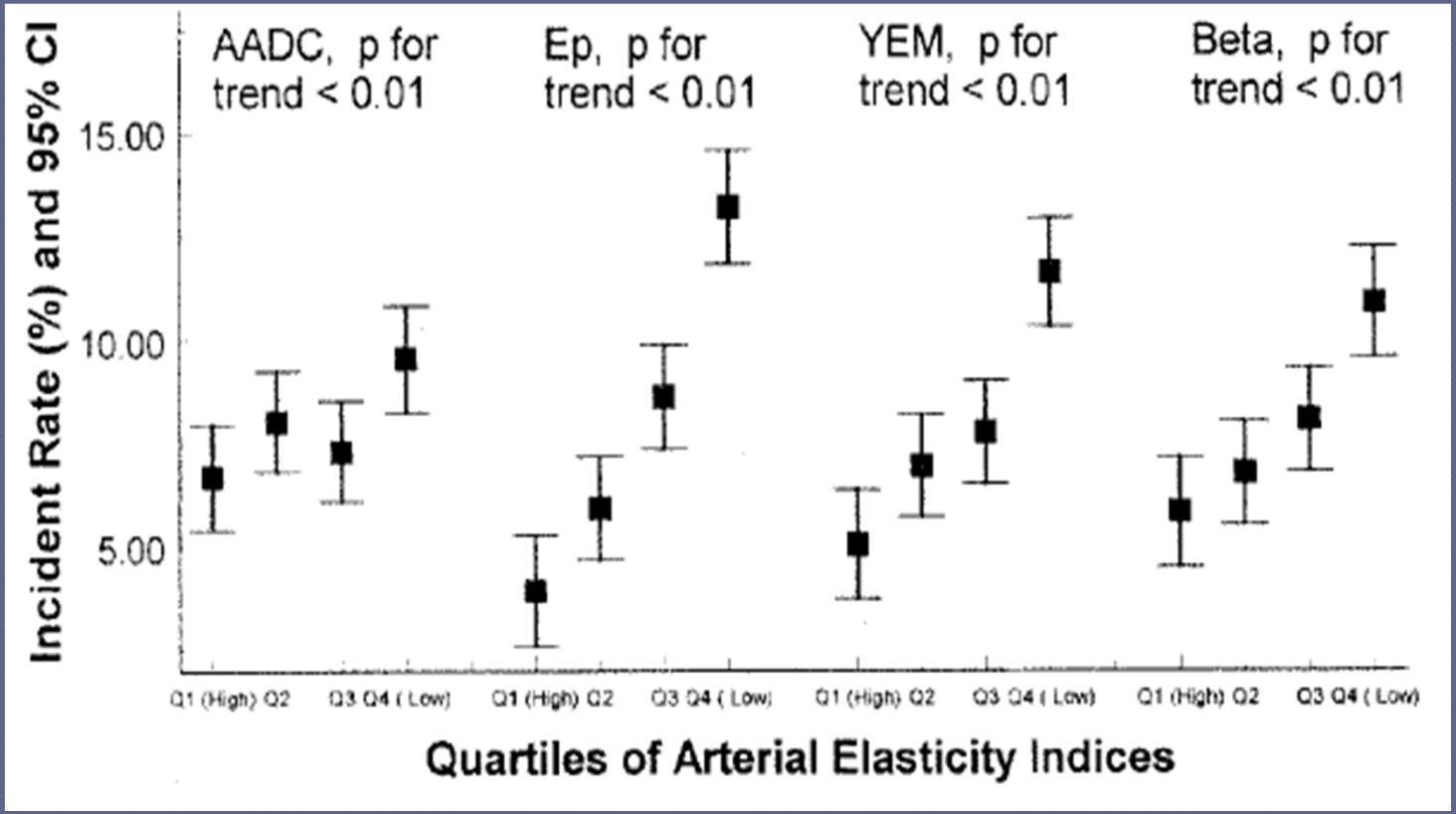
	Scoring Results : Agatston Score Protocol	
	LAD	Total Coronaries
Score	35.19	35.19
#ROI's	1	1
AreaSq (sq.mm.)	10.56	10.56

Database Match:Female, 70-100Y Percentile:42%

AV sclerosis and MAC



Arterial elasticity



Arterial stiffness and the development of hypertension: the ARIC Study.
Hypertension 1999;34:201–206

Echocardiographic evaluation of left ventricular end-systolic elastance in the elderly

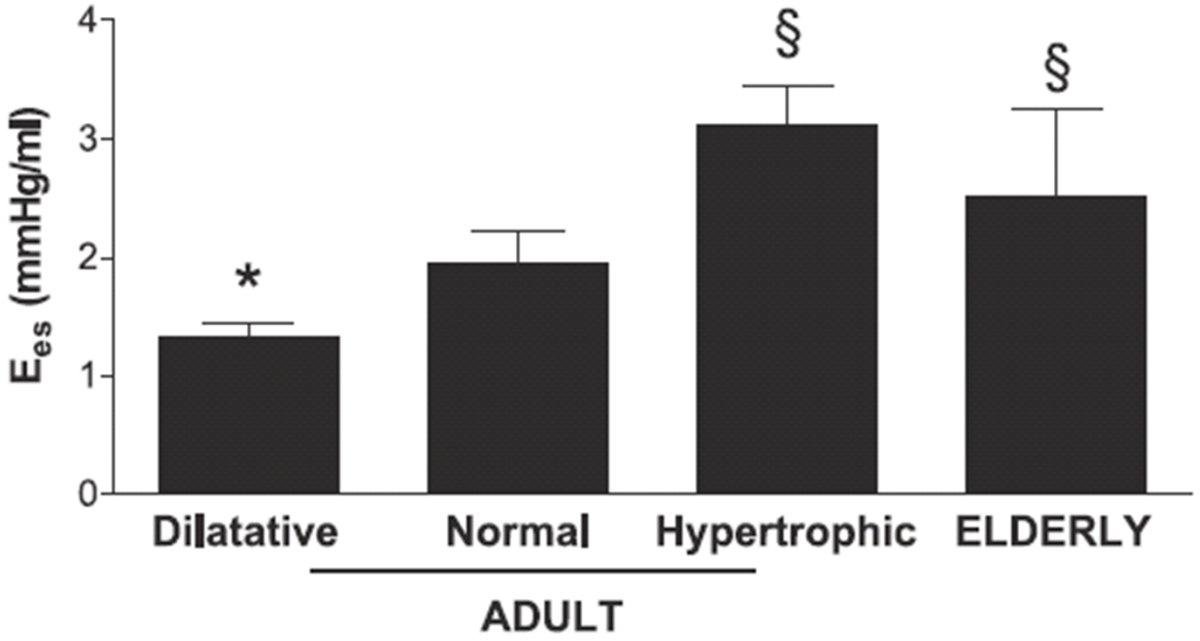
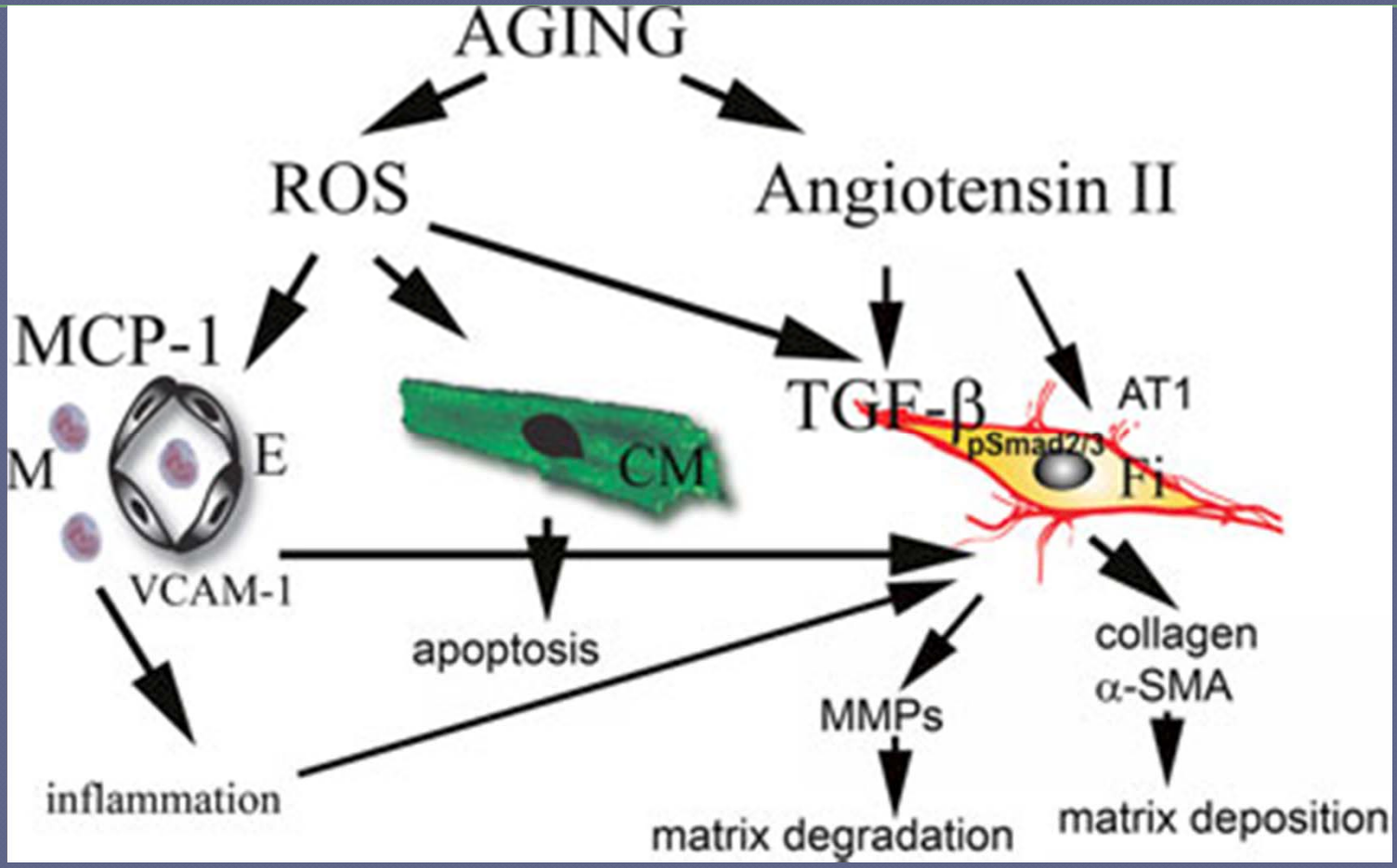


Fig. 1. Left ventricular end-systolic elastance (E_{es}) in the dilated cardiomyopathy, control, hypertensive cardiomyopathy and elderly groups (*p<0.01 vs. all groups; $^{§}p$<0.05 vs. adult control).

The European Journal of Heart Failure (2005)

The role of inflammatory and fibrogenic pathways in heart failureassociated with aging

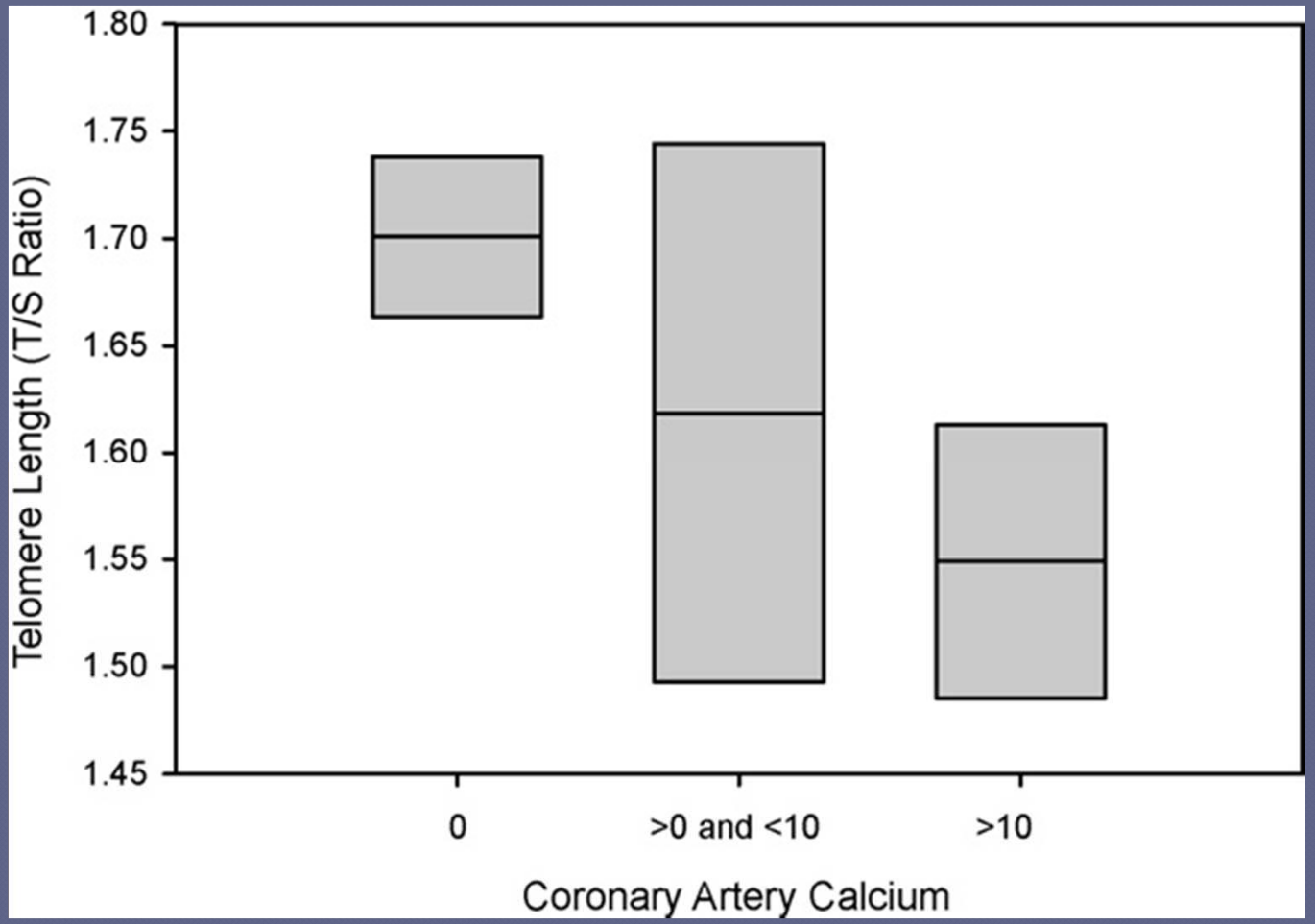


Pathways involved in the pathogenesis of cardiac fibrosis in the senescent heart

Genetic or Biomarkers of Atherosclerosis and Inflammation

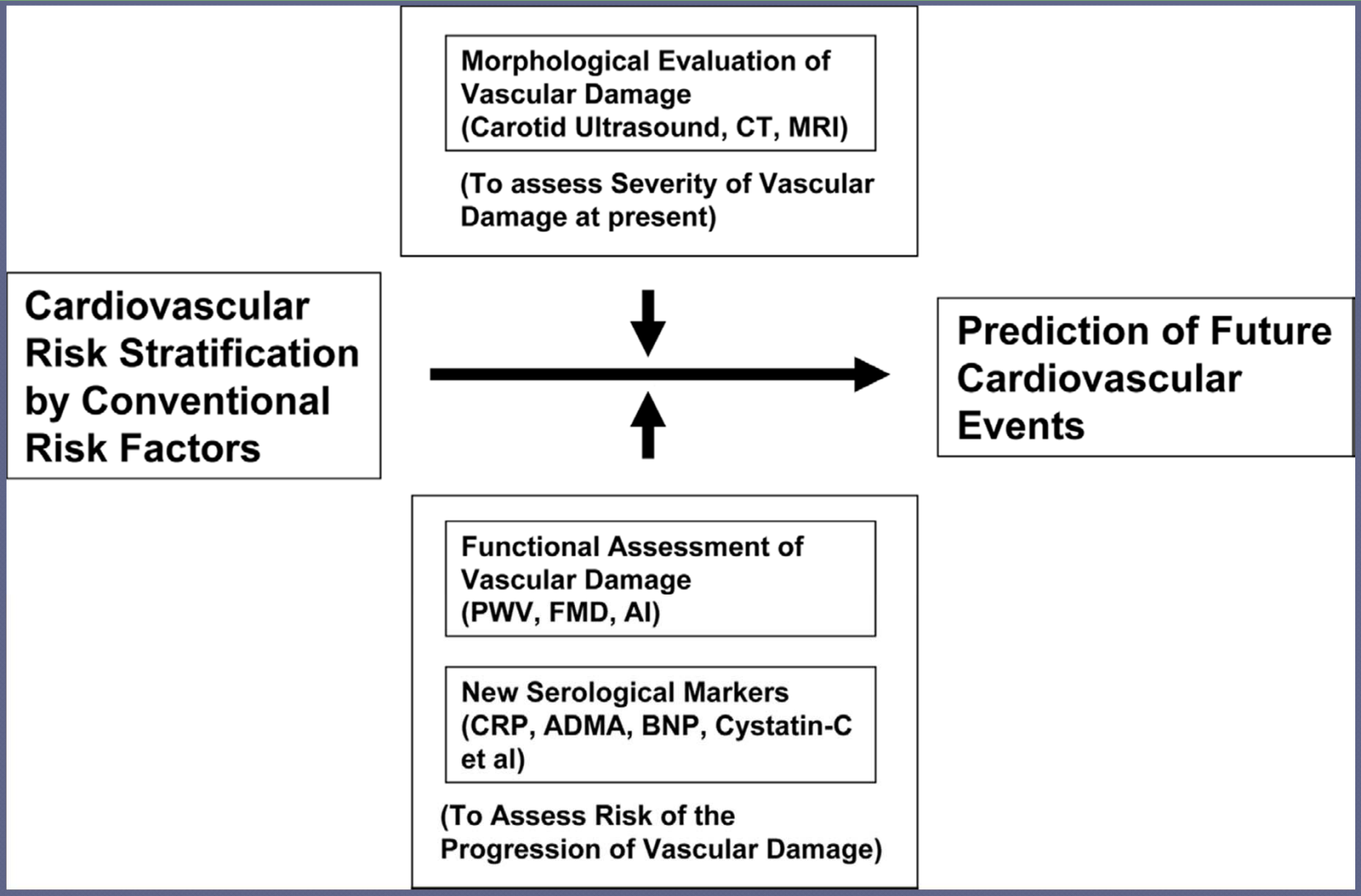
- C-reactive protein (CRP), interleukin-6 (IL-6), and tumor necrosis factor-a (TNF-a)
- Adhesion molecules
- Telomere length
- Oxygen free radical
- Extracellular matrix

Telomere Length, CAC



Arterioscler Thromb Vasc Biol. 2010;30:1649-1656.

Cardiovascular risk stratification



Aging and HF

1. Aging is associated with a progressive increase in the prevalence of CAD, HT and DM, resulting in the development of ischemic, hypertensive or diabetic cardiomyopathy.

2. Cardiac aging is linked with the development of LVH and fibrosis, leading to diastolic dysfunction and HFPEF

3. Aging-associated changes in other organ systems may affect cardiac pathophysiology contributing to the pathogenesis of heart failure.

4. Aging heart exhibits defective responses to cardiac injury, leading to accentuated adverse remodeling and increased dysfunction

Cohorts for Heart and Aging Research in Genomic Epidemiology (CHARGE)

- the Age, Gene/Environment Susceptibility (AGES) --Reykjavik Study
- the Atherosclerosis Risk in Communities (ARIC) Study
- the Cardiovascular Health Study (CHS)
- the Framingham Heart Study (FHS)
- the Rotterdam Study (RS)

- Incident events: MI, stroke, TIA, HF, PVD, Mortality, Dimentia
- Subclinical features: echo., Holter, ECG, cardiac MRI, Carotid IMT,, cerebral MRI, coronary Ca, ABI, Abd Aortic US, Bone density, endothelial function, vessel wall stiffness, PFT, sleep studies, retinal photography,
- Traditional risk factors: DM, HT, AF, BP, Lipids, FBS, GTT, smoking, medication, Ht/Wt, cognitive fn, depression, QoL, Physical activity, renal fn, biomarkers

경청해 주셔서
감사합니다.