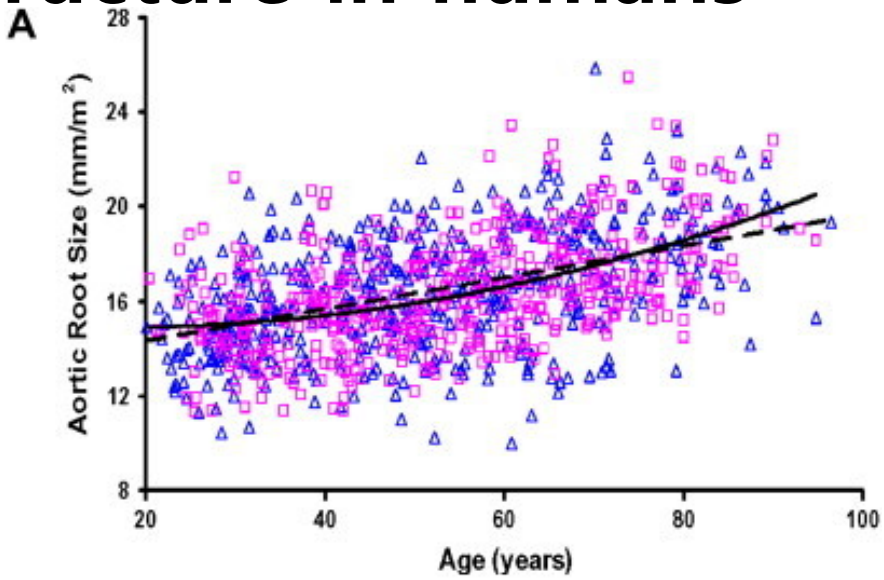
Markers of Vascualr Aging: Arterioscleosis

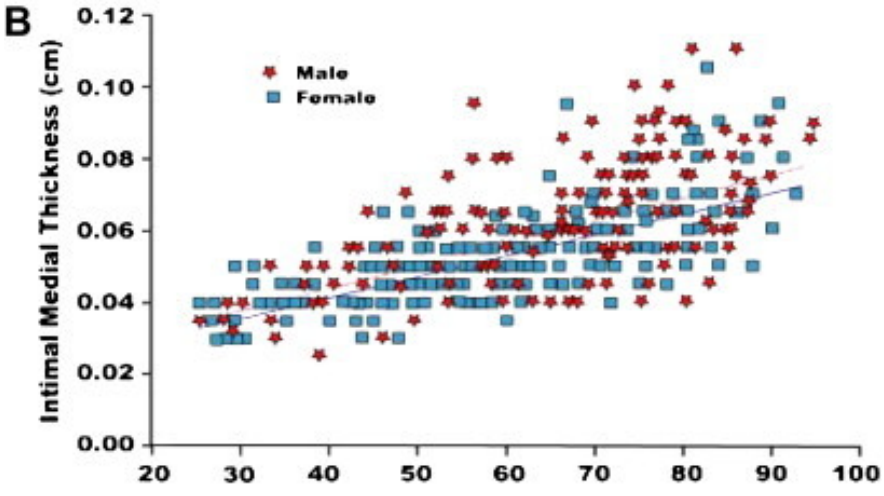
충북의대
김 동운

Age-associated macroscopic changes in central arterial structure in humans

A. Lumenal dilation



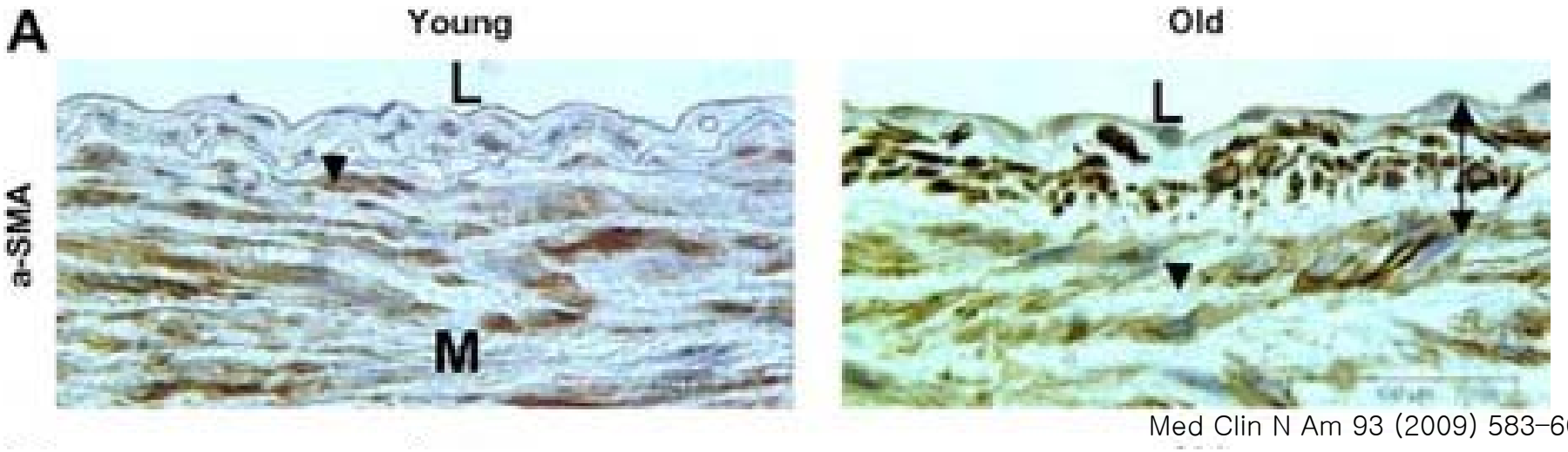
B. Diffuse intimal and medial thickening



Med Clin N Am 93 (2009) 583–604

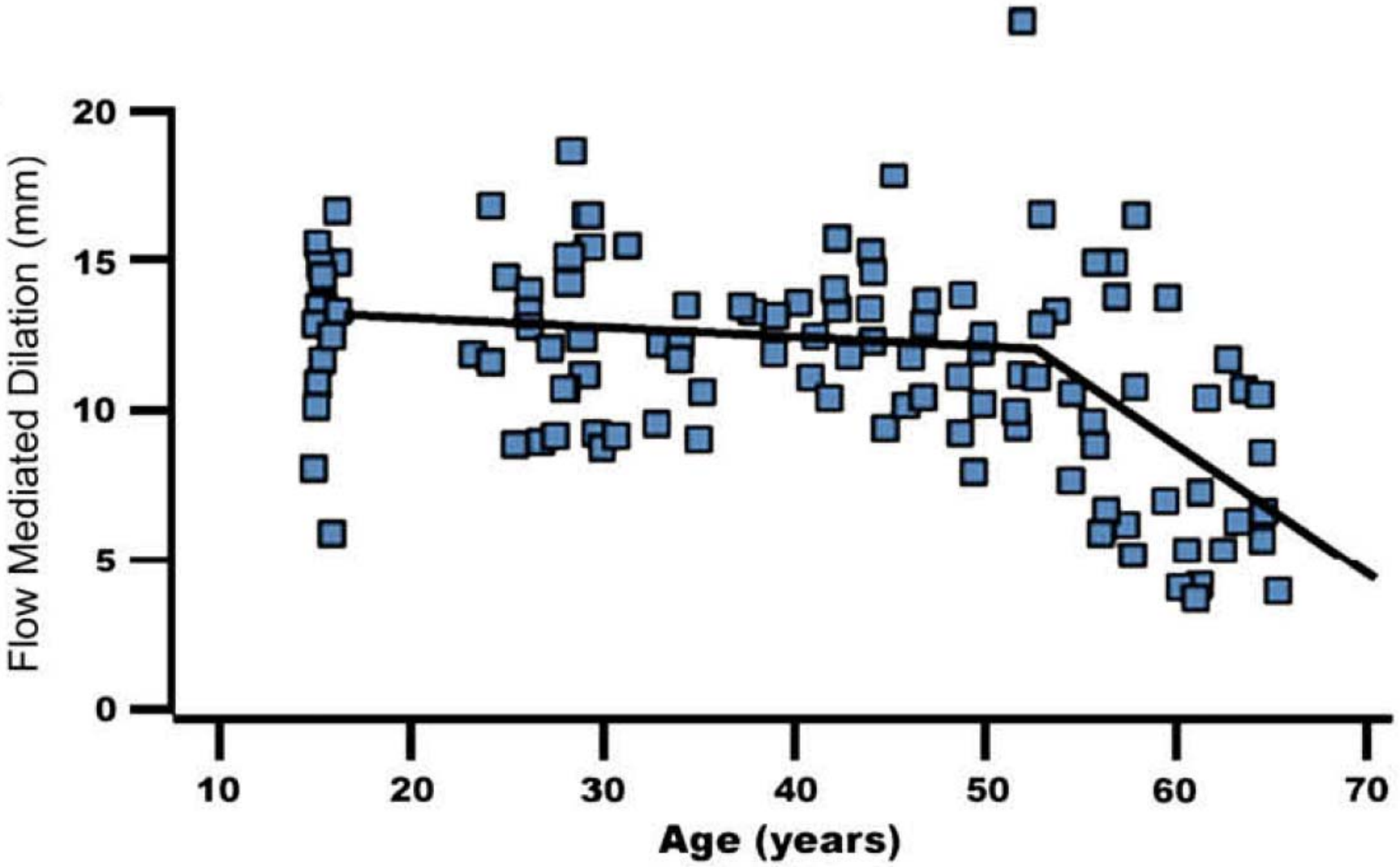
Age-associated aortic structural remodeling

- Intimal thickening
- Increased VSMC cellularity



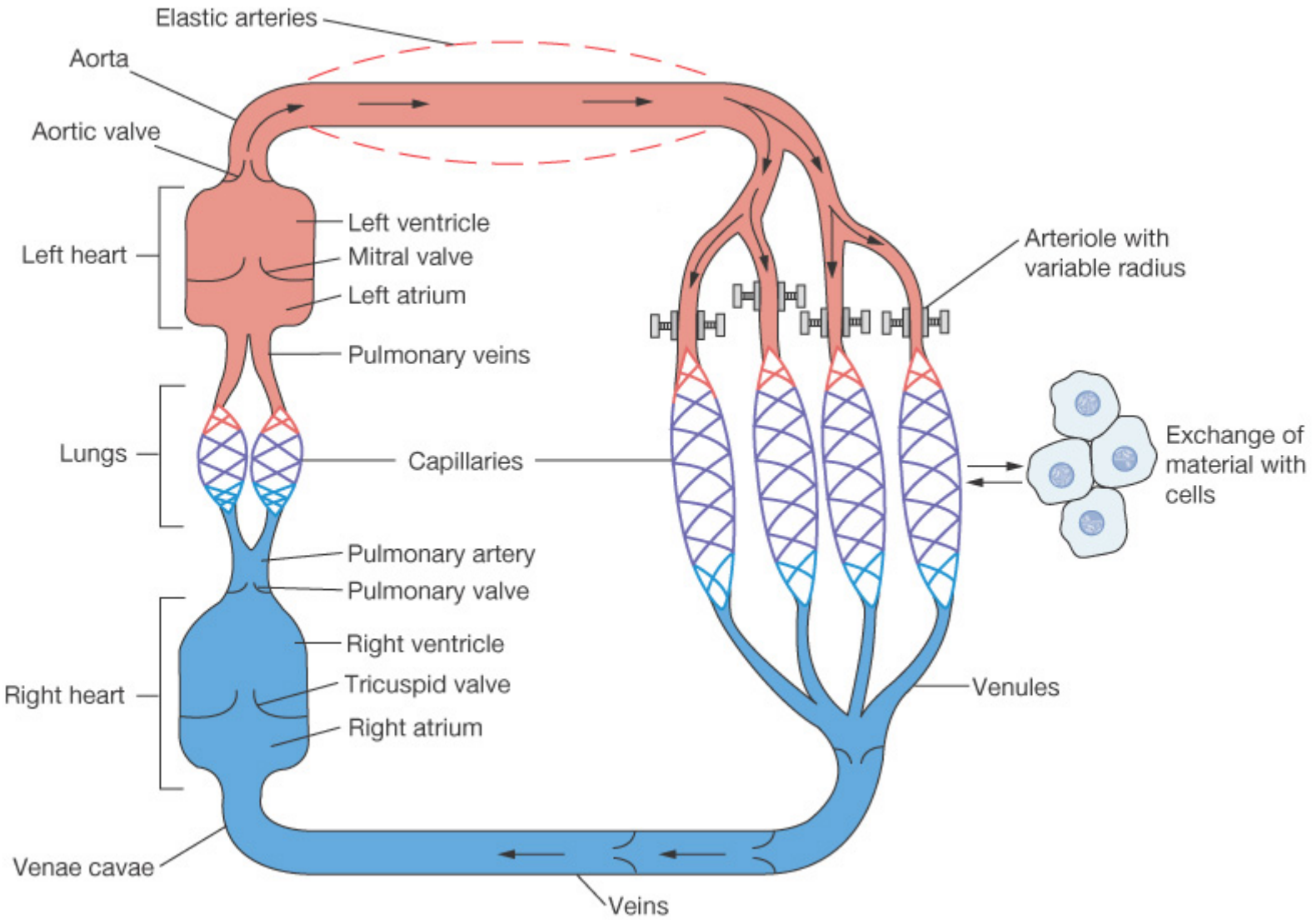
Med Clin N Am 93 (2009) 583–604

Flow-mediated induced
dilation in the brachial artery of apparently healthy women

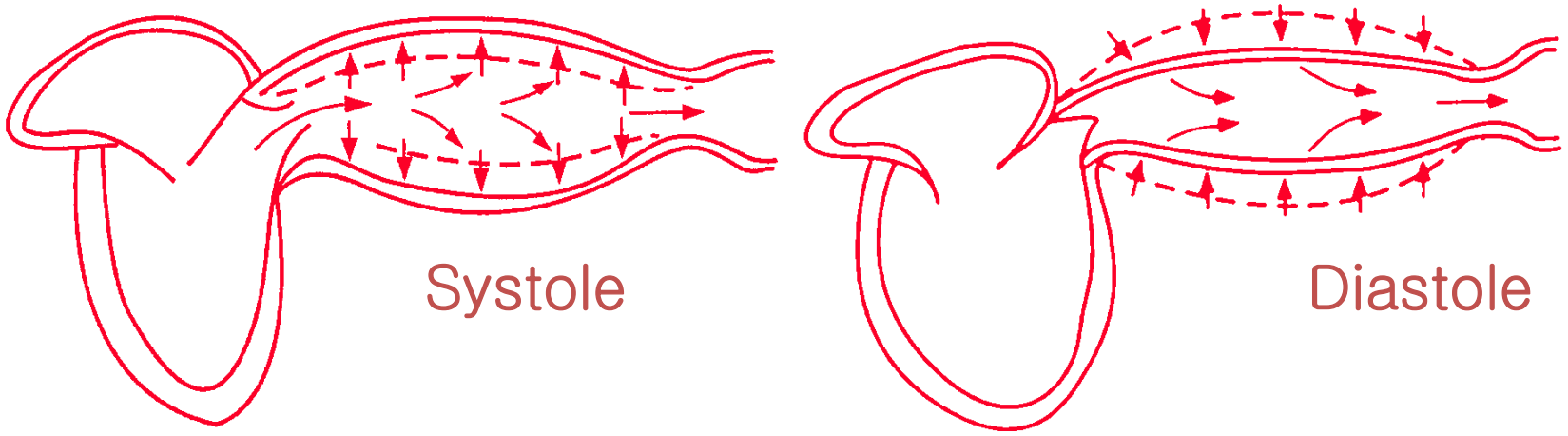


J Am Coll Cardiol 1994;24(2):471-6

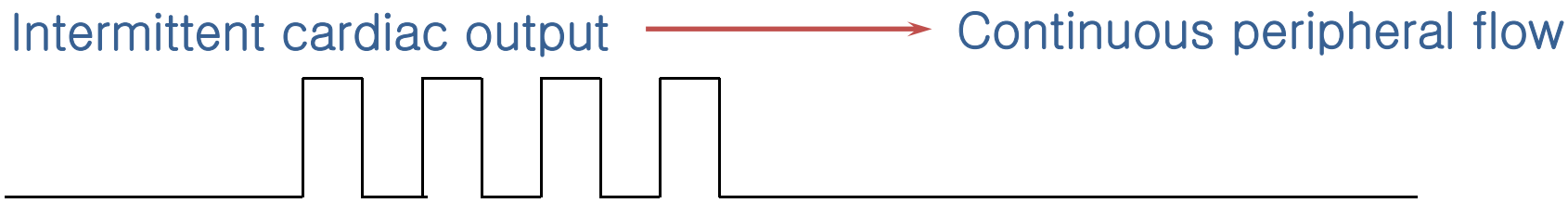
The Blood Vessels and the Cardiovascular System



Arterial Buffering function

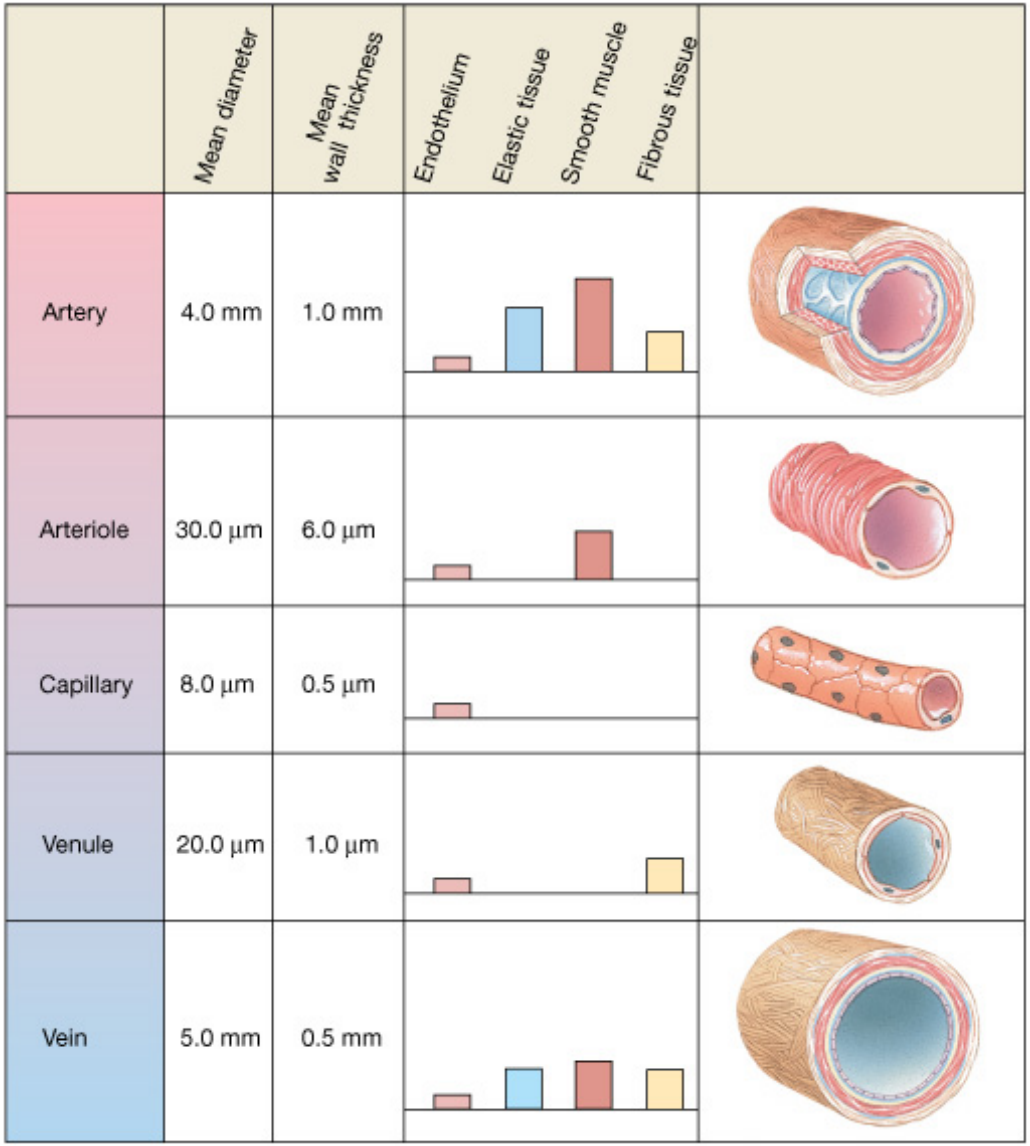


Large arteries store a part of the ejection volume during systole and restore it during diastole.



Make Up of Blood Vessels: Arteries and Arterioles

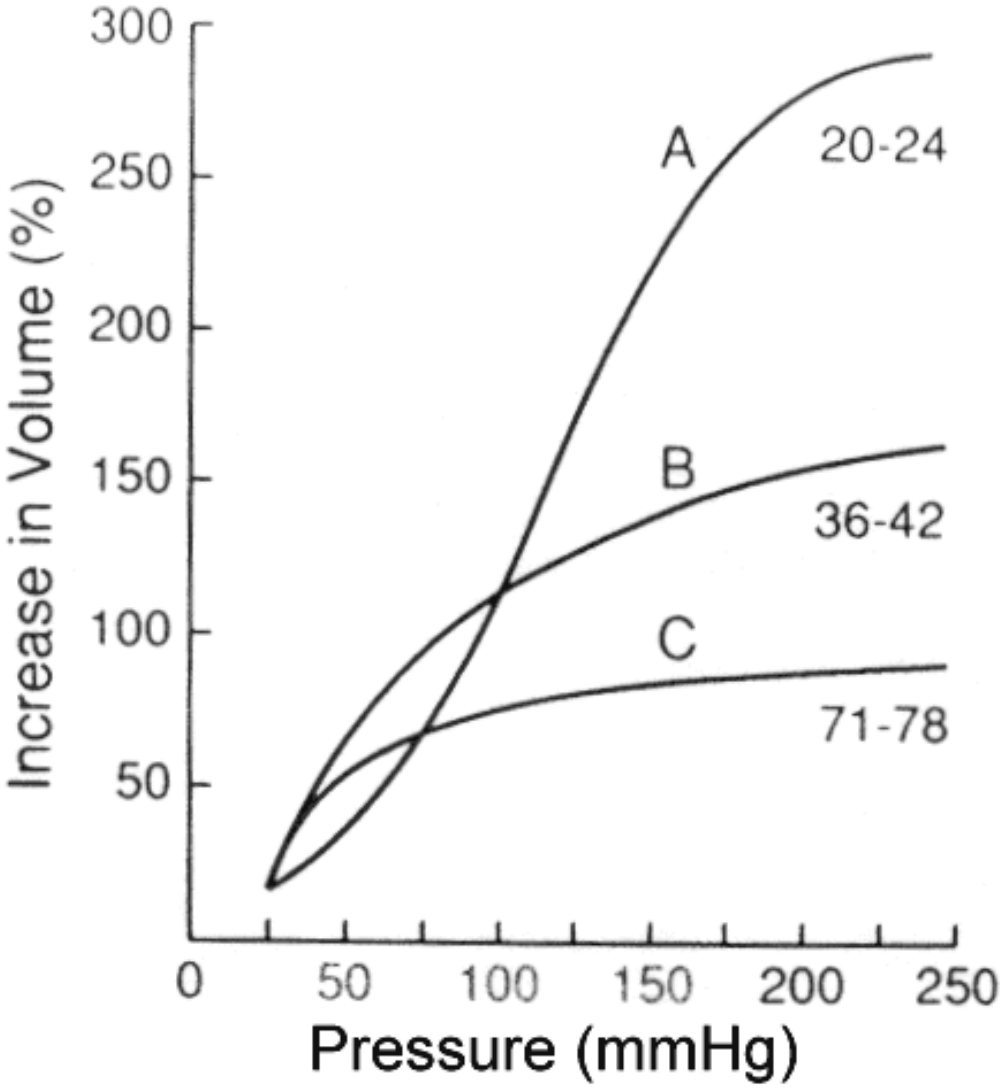
- Endothelium
- Elastic tissues
  - Rebounds
  - Evens flow
- Smooth muscles
- Fibrous tissue
  - Tough
  - Resists stretch



Definitions

- Compliance $\Delta V / \Delta P$
  - The absolute change in vessel size (volume) for a given change in pressure
- Distensibility $\Delta V / (\Delta P - V_0)$
  - The relative change in vessel size for a given change in pressure
- Stiffness
  - Non-specific term – eventually the opposite of compliance and distensibility

Aging reduces aortic compliance



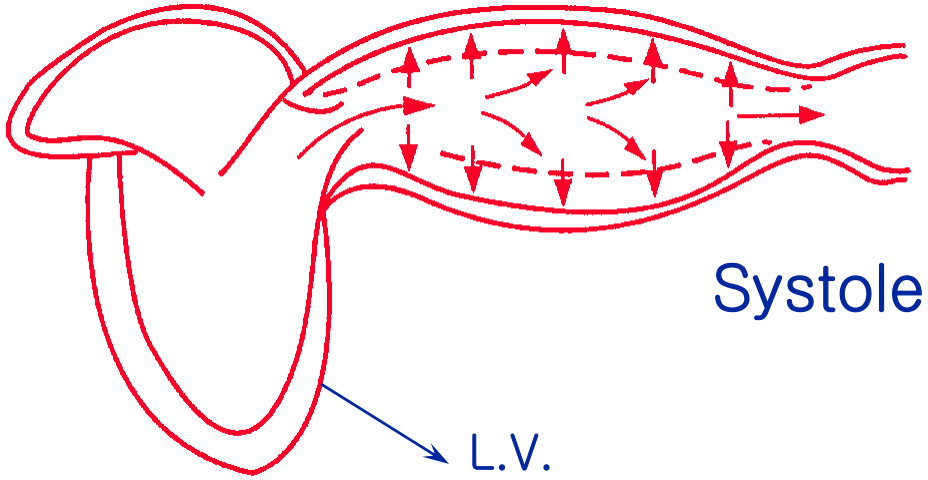
Compliance = Δ volume/Δ pressure

PULSE WAVE VELOCITY

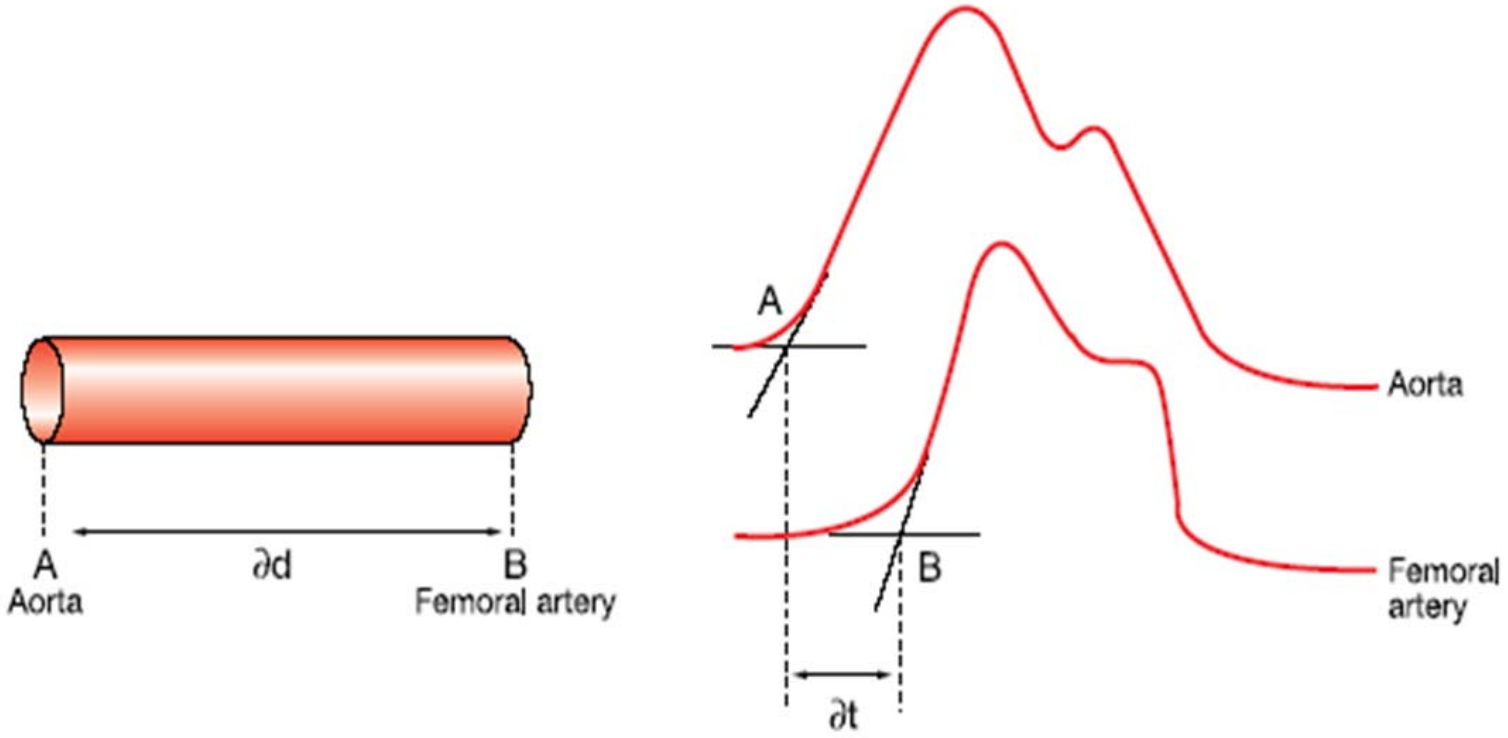
Ejection of blood into ascending aorta generates a pressure wave traveling along the arterial wall at a certain speed.

Blood = incompressible fluid
Artery = elastic conduit

} ⟹ Propagation along the arterial tree



PULSE WAVE VELOCITY



PWV = Distance (D) / Time delay (ΔT) m/sec

Usually measured over 10 heart beats.

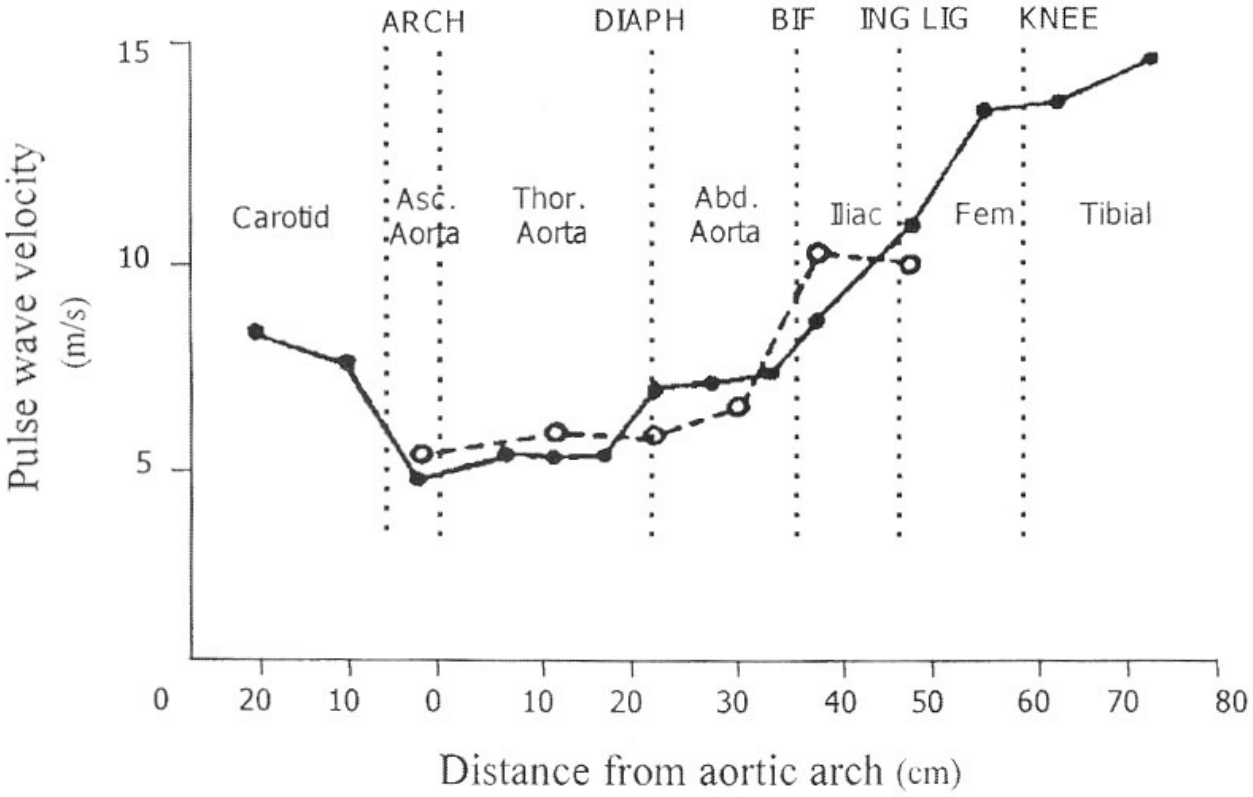
PULSE WAVE VELOCITY

- The propagation velocity is determined by:
  - **the elastic and geometric properties of the arterial wall**
  - **the characteristics of the arterial wall structure.**

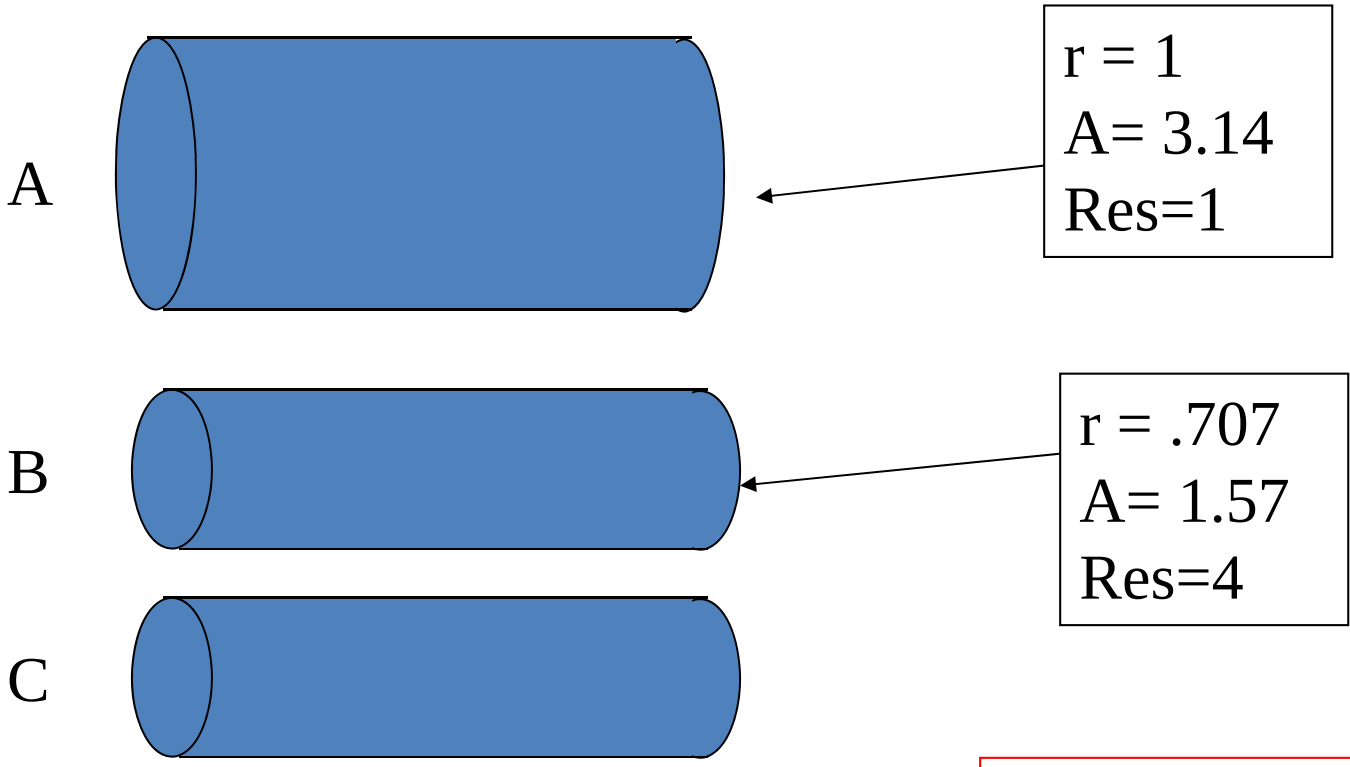
Higher velocity = higher stiffness
= lower distensibility.

PWV in Different Arteries

- Progressive increase in PWV with increasing distance from the heart in animals (solid line) and humans (dashed line).



Branching to smaller radius vessels increases resistance

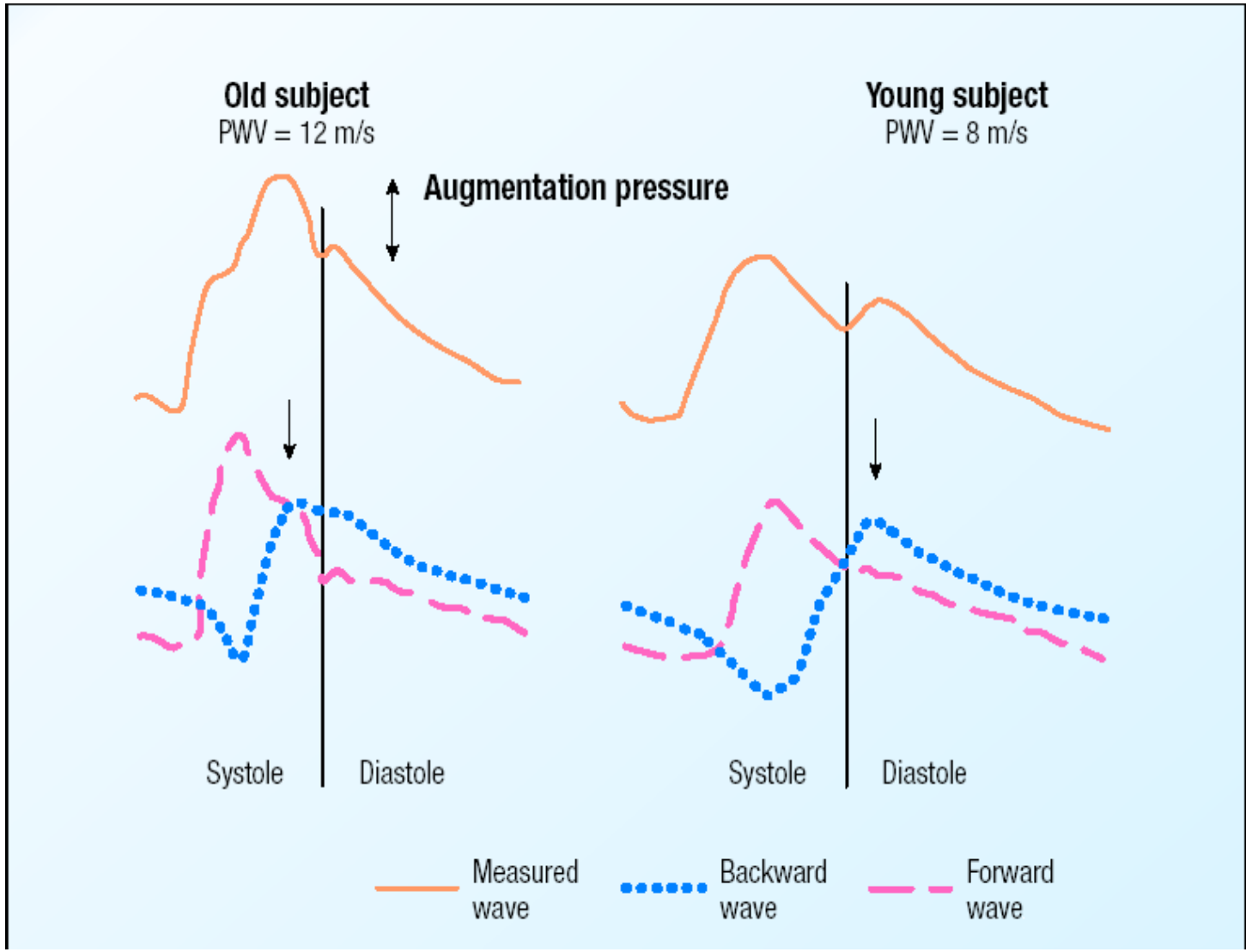


$$\text{Resistance} \sim (r^4)$$

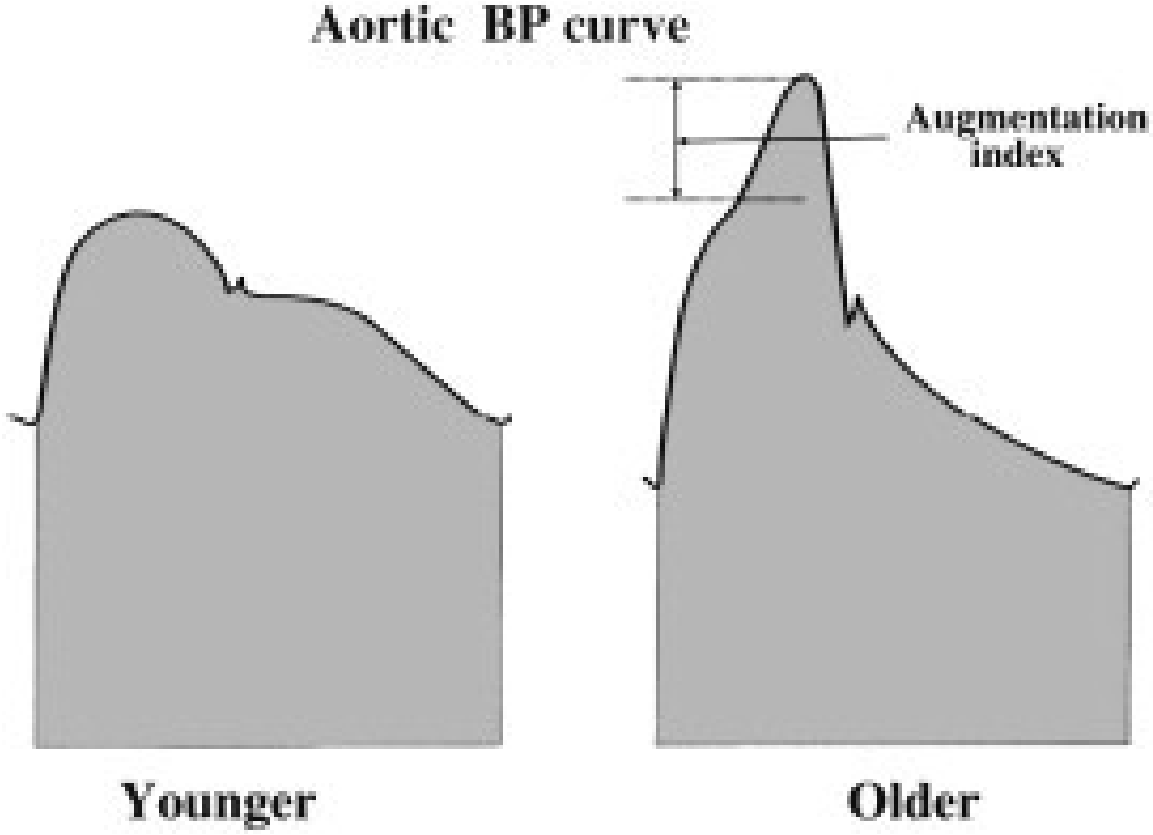
$$\text{Area} \sim (r^2)$$

B and C in parallel have a combined resistance of 2 and a cross sectional area of 3.14

Properties of Pressure Wave



Augmentation index (Aix)



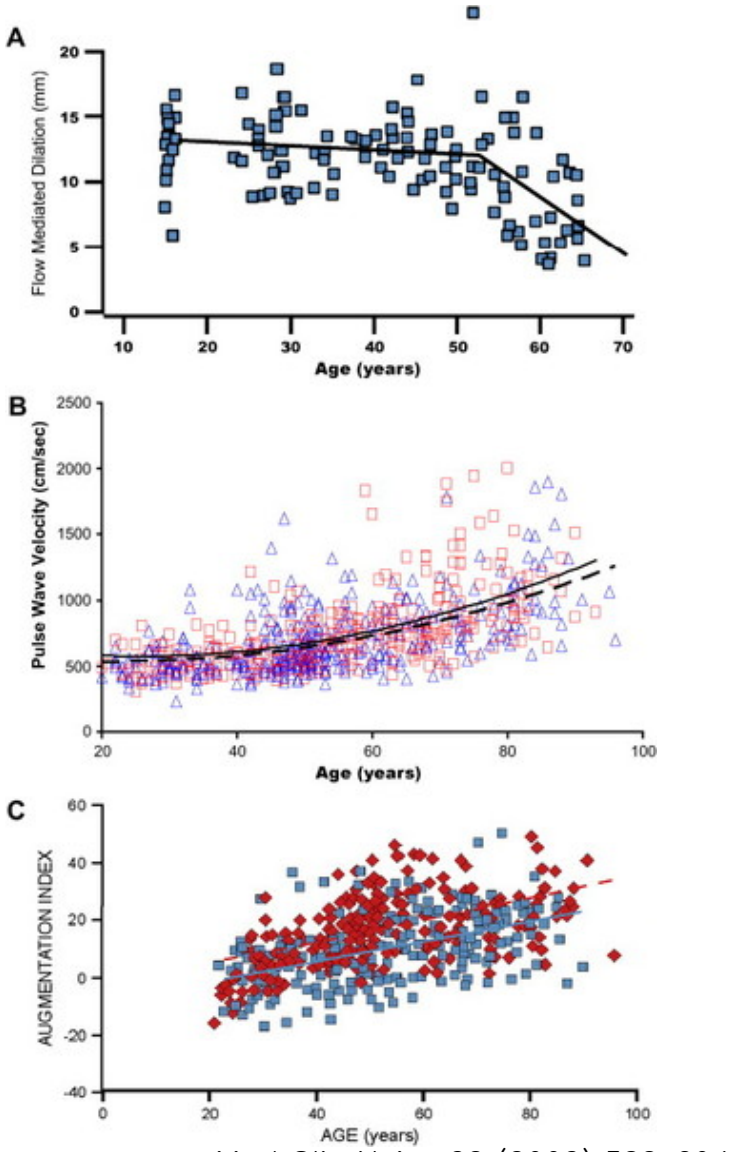
Med Clin N Am 93 (2009) 605–619

Age-associated changes in arterial function in humans

A. Flow-mediated induced dilation in the brachial artery

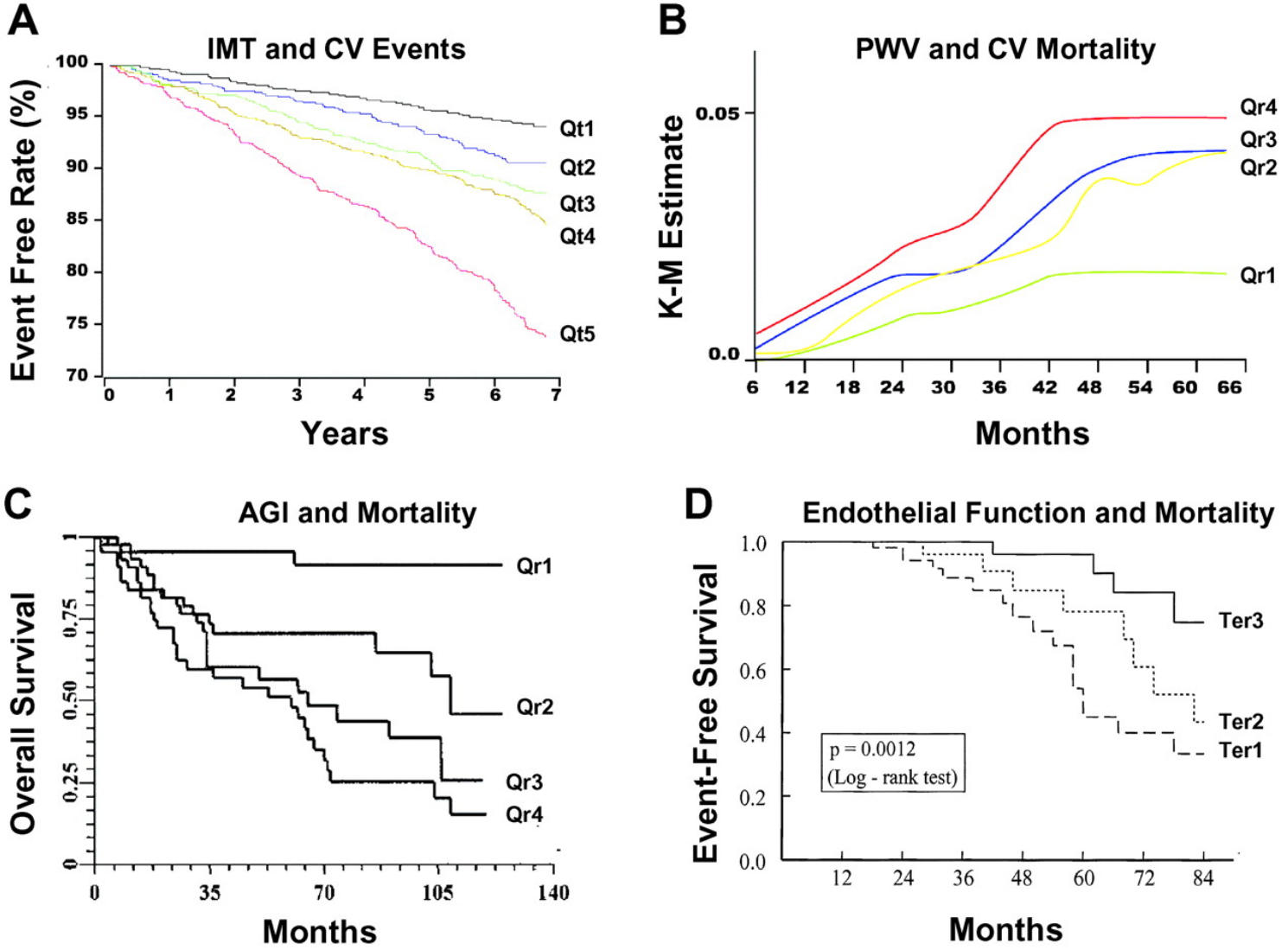
B. Age-associated increase in carotid-femoral PWV

C. Age-associated increase in augmentation index



Med Clin N Am 93 (2009) 583–604

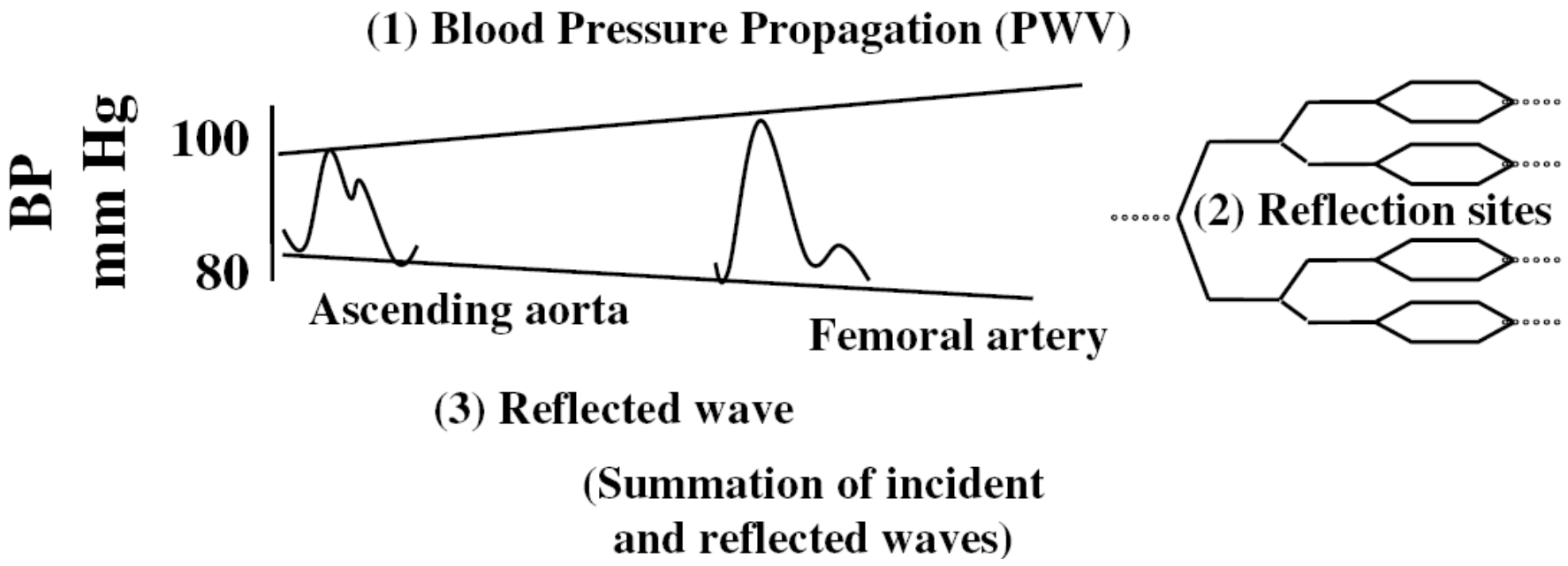
Markers of arterial aging are risk factors for adverse cardiovascular (CV) outcomes



Hypertension 2005;46;454-46

Progression of the pressure wave along the arterial tree

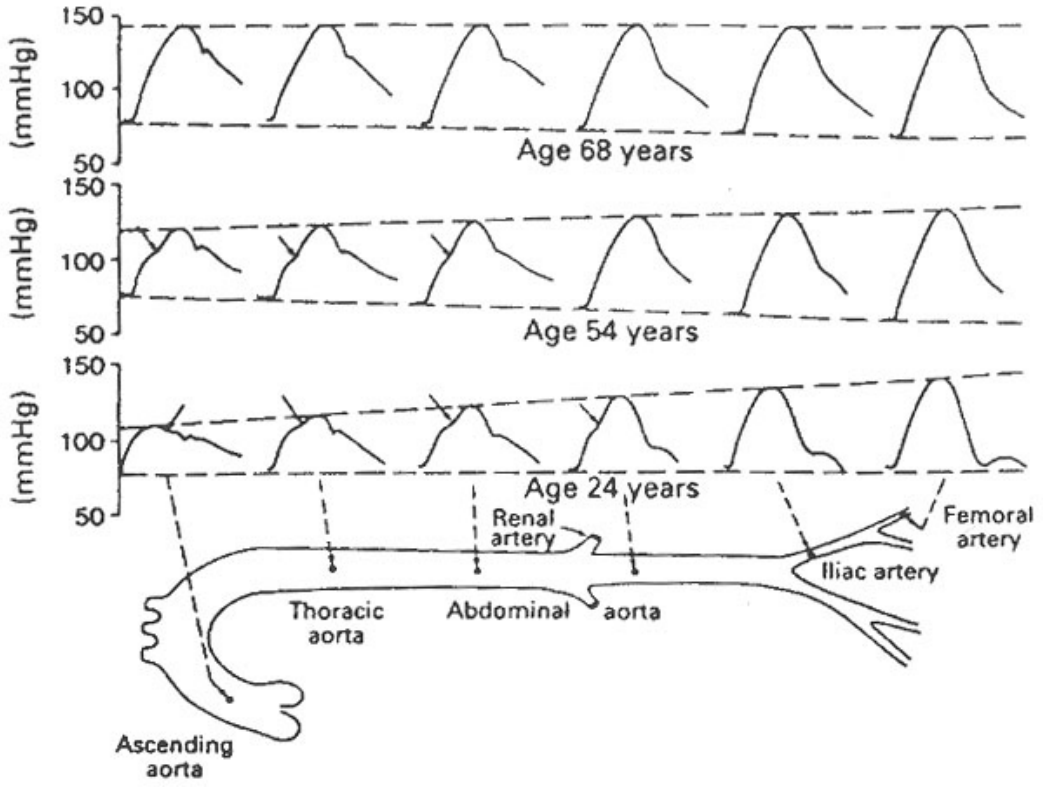
WAVE TRAVELING



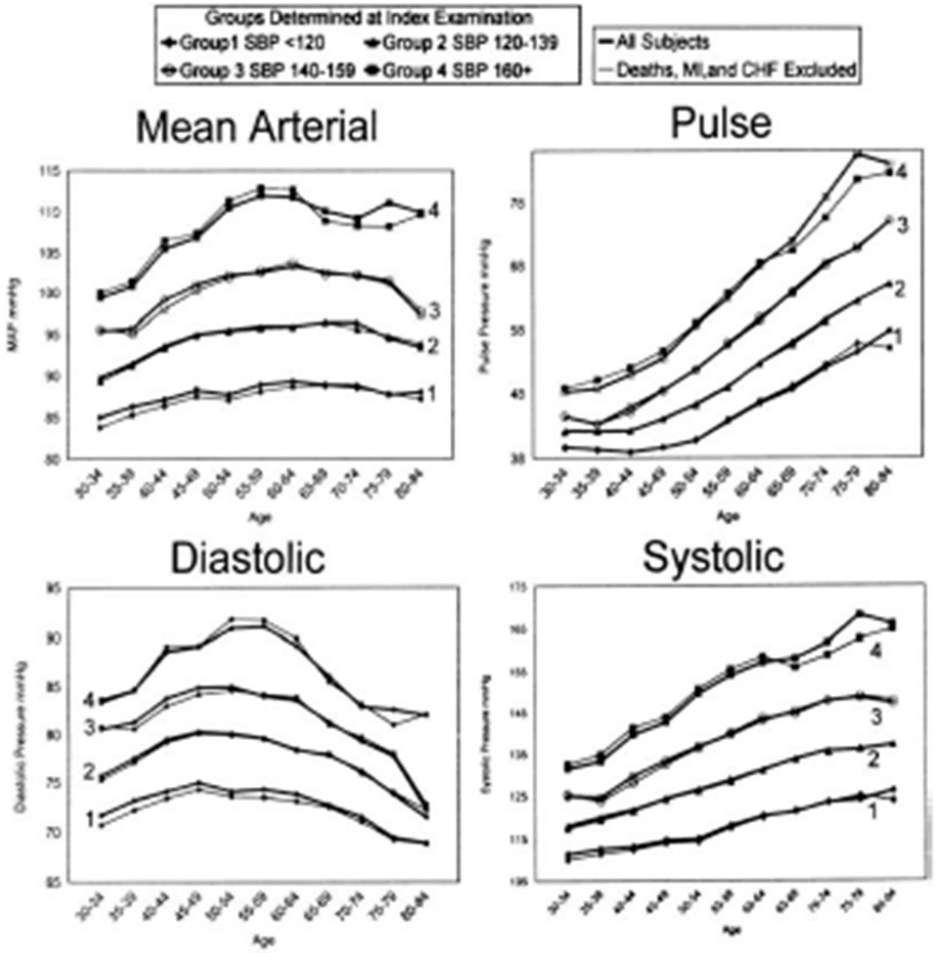
Med Clin N Am 93 (2009) 605–619

Changes of Pressure Pulse Wave with Age

- Pressure wave recorded in different sites in three adult subjects

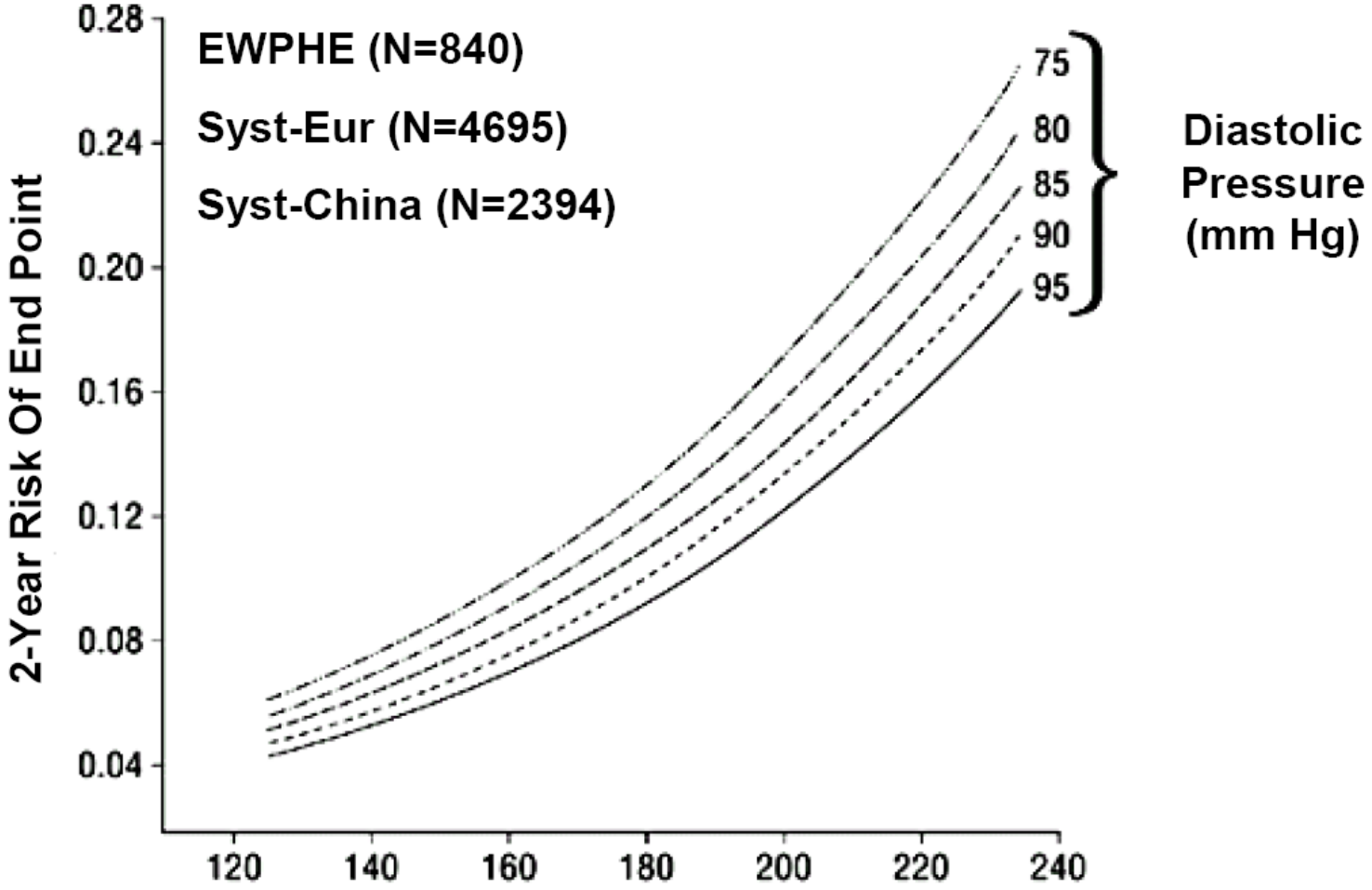


Hemodynamic patterns of age-related changes in blood pressure



Franklin et al. Circulation 1999:100:354.

Pulse Pressure
Predicts Risk Best In Older Hypertensives



Blacher et al. Arch Intern med. 2000:160

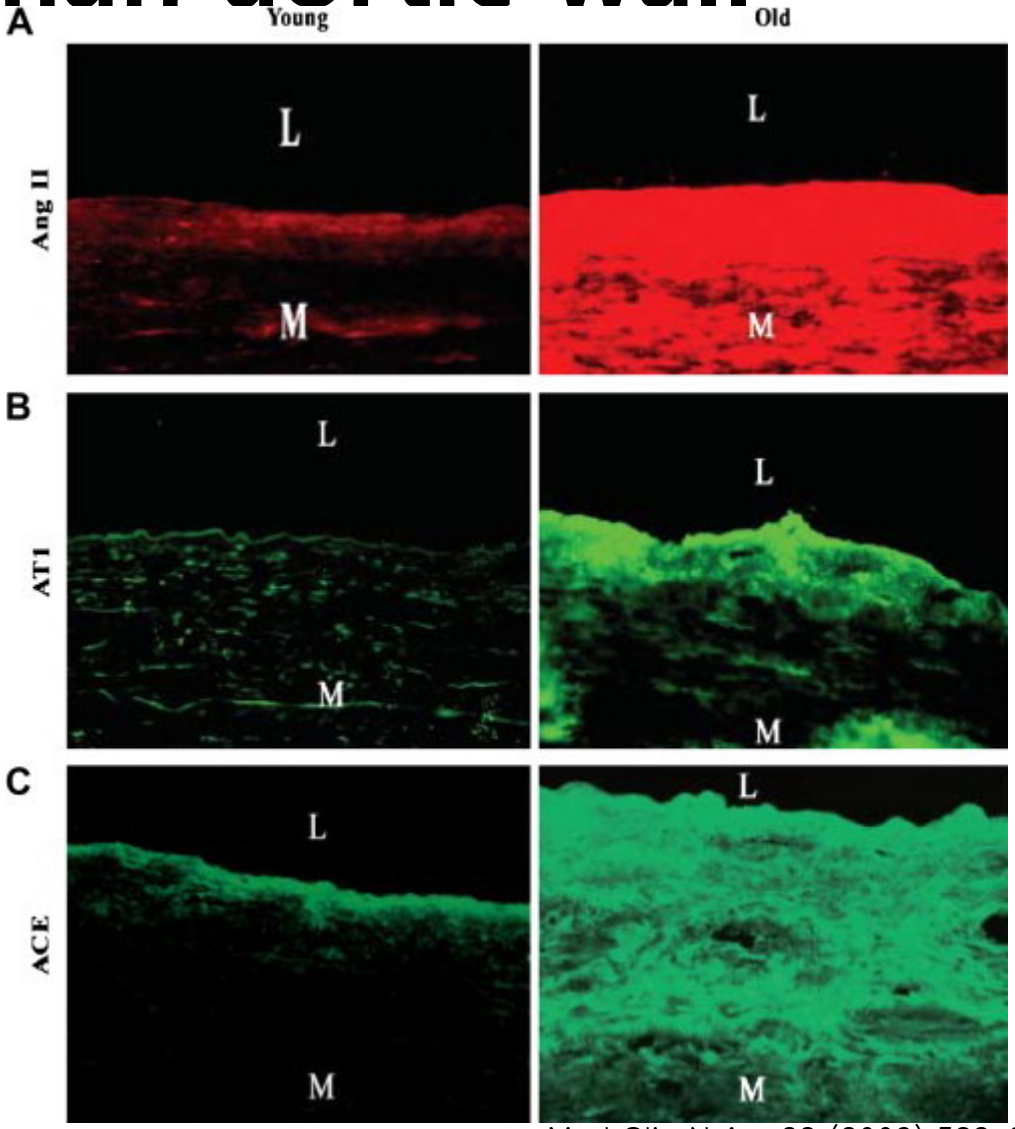
Normal Vascular Aging: ACCT trial

- **Peripheral and central pulse pressure, AP, AI, and aortic and brachial PWV all increased significantly with age**
- **Age-related changes in AI and aortic PWV were non-linear**
  - **AI increasing more in younger individuals**
  - **Changes in PWV were more prominent in older individuals**
- **AI: more sensitive marker of risk in younger individuals**
- **Aortic PWV: more sensitive marker of risk in older individuals**

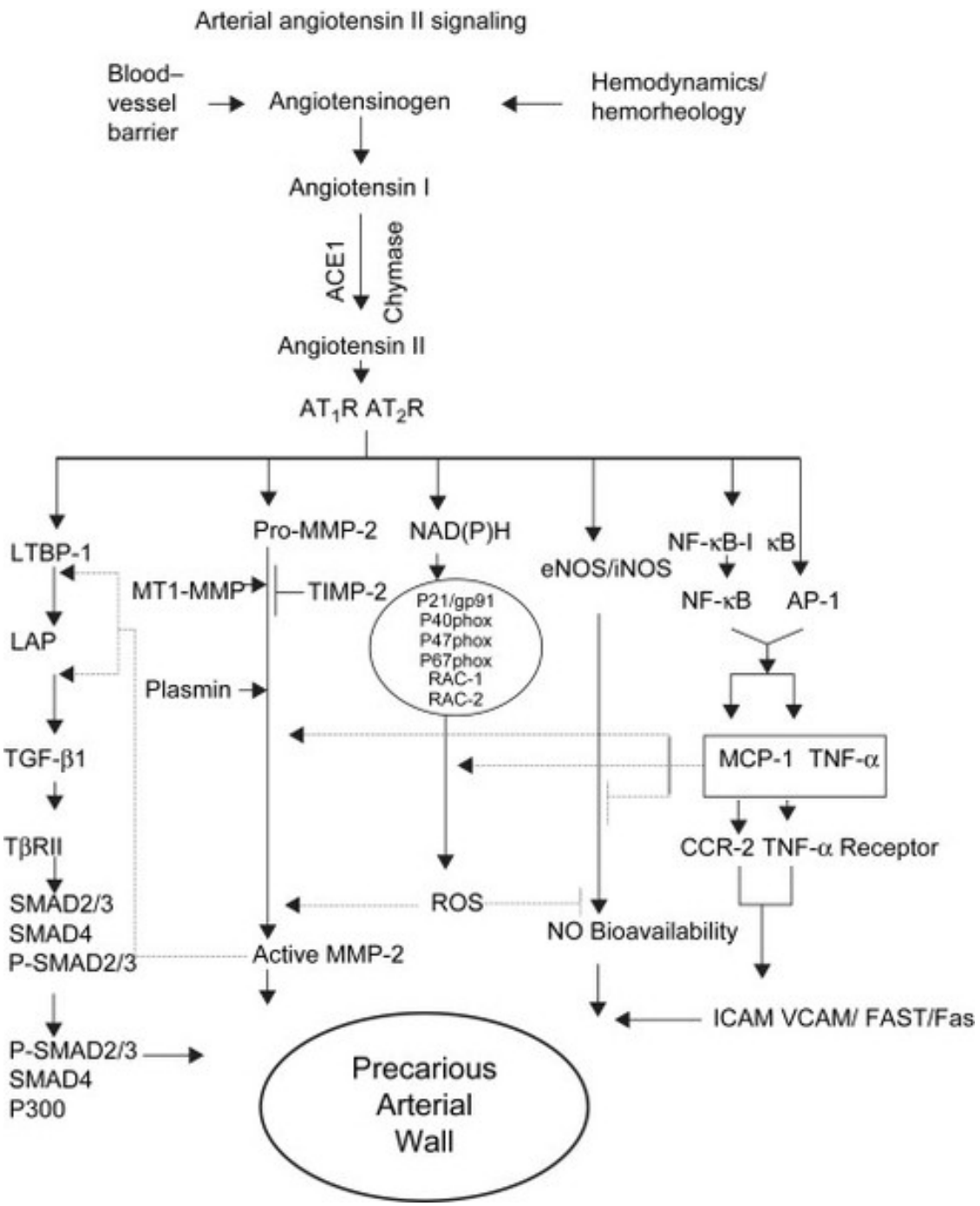
McEniery et al. ACCT trial. J Am Coll Cardiol 2005

Components of the RAS in the human aortic wall

- Arterial function is governed by age-associated changes in several signaling cascades, most prominently the renin-angiotensin system (RAS).
- The local Ang II concentration is more than 1000-fold that of circulating Ang II.
- Ang II is independently regulated, and plays an important role in vascular pathophysiology with aging.
- Elements of the classic RAS are all up-regulated in the aged arterial wall.



Med Clin N Am 93 (2009) 583–604



- The molecules linked to the Ang II signaling cascade are up-regulated within the aged arterial wall.

- Calpain-1
- MMP-2, MMP-9
- MCP-1/CCR-2
- TGF-β1

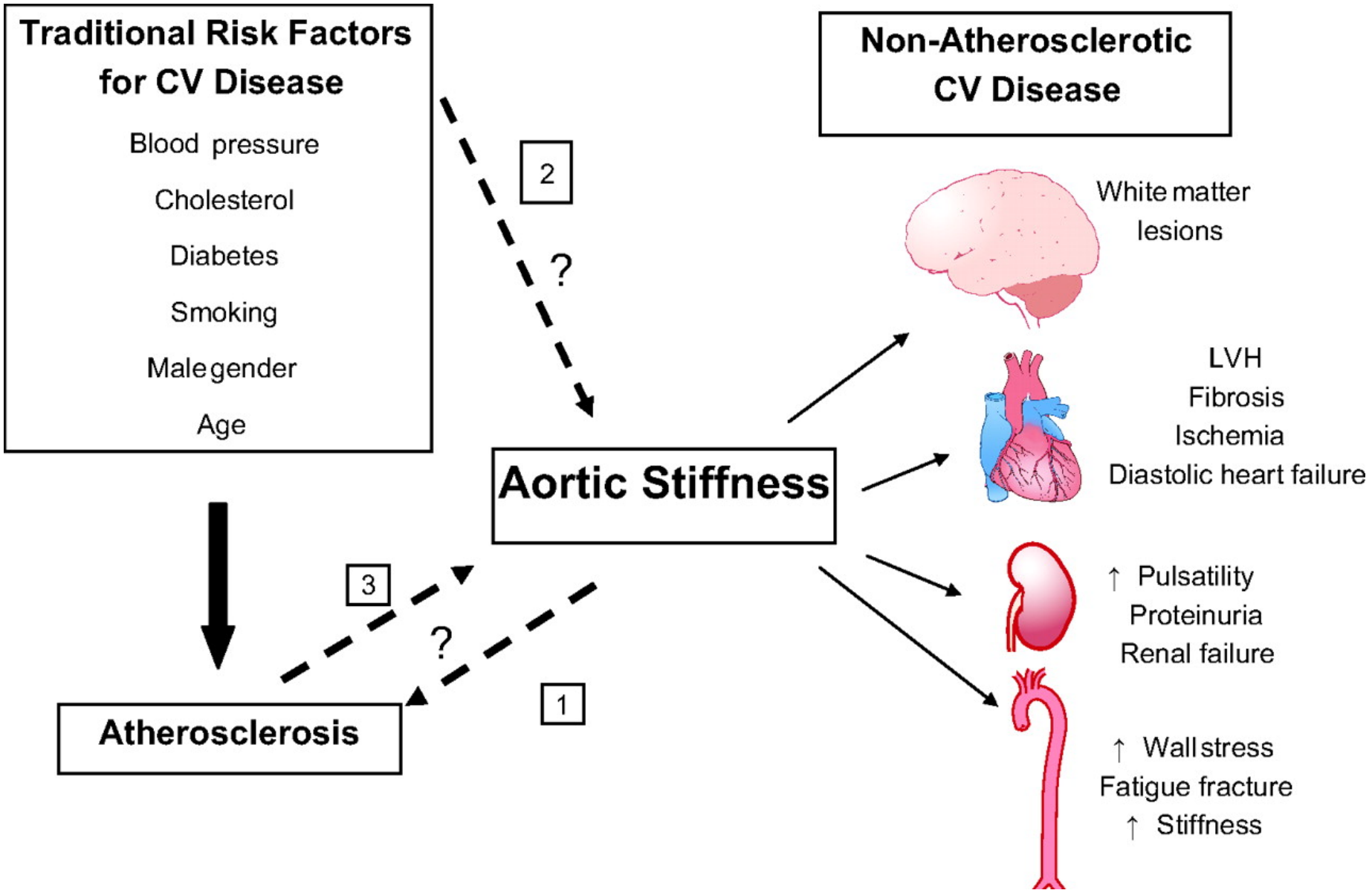
Med Clin N Am 93 (2009) 583–604

Vascular aging and Atherosclelosis

	Vascular Aging	Atherosclelosis
Luminal dilation	+	?
↑ Stiffness	+	?
↑ Collagen	+	?
↓ **Elastin**	+	?
Endothelial dysfunction	+	+
Diffuse intimal thickening	+	+
Lipid involvement	−	+
↑ **VSMC number**	+	+
Macrophages	+	+
T cells	+	+
↑ **Matrix**	+	+
↑ **Local Ang II-ACE**	+	+
MMP dysregualtion	+	+
↑ **MCP-1/CCR2**	+	+
↓ **VEGF**	+	+
↓ **Telomere length**	+	+

Modified from Najjar SS et al. *Hypertension*. 2005;46:454-462

Proposed mechanisms linking aortic stiffness with atherosclerotic and nonatherosclerotic cardiovascular disease



Wilkinson, I. B. et al. Hypertension 2009;54:1213–1215