Markers of Vascular Aging: Arteriosclerosis

충북의대
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Age-associated macroscopic changes in central arterial structure in humans

A. Lumenal dilation

B. Diffuse intimal and medial thickening
Age-associated aortic structural remodeling

- Intimal thickening
- Increased VSMC cellularity
Flow-mediated induced dilation in the brachial artery of apparently healthy women
The Blood Vessels and the Cardiovascular System
Large arteries store a part of the ejection volume during systole and restore it during diastole.

Intermittent cardiac output  →  Continuous peripheral flow
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 = $\Delta$ volume/$\Delta$ 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

Blood pressure wave propagates along the arterial tree during systole.
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

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

Resistance \sim (r^4)
Area \sim (r^2)
Properties of Pressure Wave

Old subject
PWV = 12 m/s

Young subject
PWV = 8 m/s

Augmentation pressure

Systole  Diastole  Systole  Diastole

Measured wave  Backward wave  Forward wave
Augmentation index (Aix)
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

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

(1) Blood Pressure Propagation (PWV)

BP (mm Hg)

100

80

Ascending aorta

Femoral artery

(2) Reflection sites

(3) Reflected wave

(Summation of incident and reflected waves)

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

Pulse Pressure Predicts Risk Best In Older Hypertensives

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.
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
# Vascular aging and Atherosclerosis

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<td>↑ Stiffness</td>
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<td>↓ Telomere length</td>
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Proposed mechanisms linking aortic stiffness with atherosclerotic and nonatherosclerotic cardiovascular disease

Traditional Risk Factors for CV Disease
- Blood pressure
- Cholesterol
- Diabetes
- Smoking
- Male gender
- Age

Aortic Stiffness

Non-Atherosclerotic CV Disease
- White matter lesions
- LVH
- Fibrosis
- Ischemia
- Diastolic heart failure

Atherosclerosis
- Pulsatility
- Proteinuria
- Renal failure
- Wall stress
- Fatigue fracture
- Stiffness