Clinical application of Arterial stiffness

pulse wave analysis
pulse wave velocity
Arterial system

1. Large arteries: elastic arteries
   Aorta, carotid, iliac,
   Buffering reserve: store blood during systole expel during diastole

2. Muscular arteries: lower body: femoral, popliteal, tibial, twice as long as elastic artery altering muscle tone: modify speed of pulse wave

3. Arteriole:
   change caliber—alter peripheral resistance
   maintain mean pressure
The Arterial Wall

Different arteries have different ratios of arterial wall structural components. Hypertension causes medial hypertrophy, elastin degradation, and collagen formation.

- Intima
  - endothelium
  - connective tissue

- Media
  - smooth muscle
  - protein matrix of elastin/collagen
  - internal elastic lamina

- Adventitia
  - strong, fibrous tissue to maintain vessel shape

Arterial Stiffness
△ PP

Vascular endothelial damage & mechanical fatigue

△ Central Wave Reflection

△ Aortic Stiffness

△ Atherosclerosis
Arterial Stiffness

There are three separate processes increasing stiffness in the arterial system:

- **Structural Breakdown of Elastin Fibers**
  - occurs primarily in the aorta
  - age driven (cum. millions of cardiac cycles)

- **Damage to Endothelial Function**
  - occurs primarily in the smooth muscle conduit arteries
  - disease driven (e.g., Type II diabetes, hypercholesterolemia, atherosclerosis)

- **Increase in Mean Arterial Pressure**
  - occurs systemically throughout the arterial system.
Arterial Stiffness

CV Risk Factors such as:
- High cholesterol
- High BP
- Diabetes
- Smoking
- Aging

Cause:
Elevated Arterial Stiffness

Which in turn is the major cause of:
- Heart Failure
- Stroke
- Heart Attack
How to assess arterial stiffness

Augmentation Index

Pulse Wave Velocity
Arterial Pulse Wave
TWO PATIENTS –
  one “red”, one “black dots” – have identical cuff Sp/Dp ~140 / 80

BUT... aortic BP profile shows critical difference at the heart between patients; => Cuff BP OK for managing Dp; but NOT adequate for managing Sp and Pp.

WHY? .... We are seeing the effect of differing ARTERIAL STIFFNESS.
If there was no wave reflection (i.e., the aorta was an open-ended tube providing a simple resistance to flow), then:

- the pressure wave in the aortic root would be the same as the flow wave.
Now if we connect up the network of arteries with all its bifurcations and vascular beds, then:

- as this primary wave travels along the arteries it will generate reflected waves from each bifurcation and from the peripheral vascular beds.
- all these small reflected waves return to the heart, summing to create a reflected wave as shown, starting even before the end of systole.
So the pressure in the aortic root is the sum of the outgoing and reflected wave (the green wave).

note importantly how the reflected wave boosts the coronary artery perfusion pressure – the aortic root pressure – during diastole when over 95% of perfusion of the sub-endocardium takes place.
The speed at which the outgoing and reflected waves travel is dependent on the stiffness of the arteries along which they are travelling.

So if a person has stiffer arteries, the waves will travel out and back quicker, arriving earlier back at the heart.
Pressure Wave Reflection at the Heart

Now when the outgoing and reflected waves are added there is a very different aortic root pressure waveform.

there are three important clinical implications.
First, the central systolic pressure and central pulse pressure is increased. an increase in the central pulse pressure that drives cerebral blood flow increases stroke risk. 

NOTE: this change in central systolic pressure can occur without any changes occurring in peripheral cuff systolic pressure.
Second, there is an increase in left ventricular load (LV load).

- Increase in LV load accelerates increase in LV mass and increases risk of LV hypertrophy.
- The area under the pressure-time curve during systole is by definition LV load.
- This increase in LV Load (late systolic “afterload”) is shown by the black arrowed region.
Third, the pressure that is perfusing the coronary arteries during the critical diastole period is reduced, increasing the risk of myocardial ischemias.

Conclusion: Increasing arterial stiffness independently increases the risk of all three major cardiovascular outcomes.
Figure 3. Components of central blood pressure and cardiac afterload. Left-hand panel demonstrates the characteristics of a typical aortic pulse contour. Dicrotic notch (DN) is the division between systolic and diastole. Mean arterial pressure (MAP = diastolic blood pressure [DBP] + 1/3 pulse pressure [PP]) represents steady-state load throughout the cardiac cycle. PP (the maximal difference between systolic pressure [SBP] and DBP) represents the dynamic component. Major vascular components of central PP and cardiac afterload (right panel) include resting circulatory pressure (DBP), ventricular-aortic coupling mechanisms during early systole, and late systolic augmentation pressure (AP) caused by the return of reflected waves to the aortic root. P1, pressure peak caused by the incident flow wave; P2, pressure peak that results from the summation of incident and reflected waves. Augmentation index (AI) = AP/PP.

A much simplified arterial system with the tonometer sensor on the left at the ascending aorta and the effective reflection site at right.
A much simplified arterial system with the tonometer sensor on the left at the ascending aorta and the effective reflection site at right.

Vasoconstriction
A much simplified arterial system with the tonometer sensor on the left at the ascending aorta and the effective reflection site at right.

Vasodilation
A much simplified arterial system with the tonometer sensor on the left at the ascending aorta and the effective reflection site at right.

Stiff Artery
Aortic pressure at 18 years

Aortic pressure at 40 years

Aortic pressure at 59 years

Aortic pressure at 80 years

Incident

Reflected

200 msec
Typical waveform

Young normotensive

Note: Narrow radial peak. Late systolic shoulder in aortic pulse is lower than the early systolic peak (negative augmentation).

Middle aged normotensive

Note: Wide radial systolic peak. Late systolic peak in aortic pulse is higher than early systolic shoulder (positive augmentation).

Elderly normotensive

Note: Increased late systolic shoulder in radial pulse. Increased late systolic augmentation in the aortic pulse.

Young hypertensive

Note: Prominent late-systolic shoulder in the radial waveform. Presence of late systolic augmentation in the aortic pulse.

Middle aged hypertensive

Note: Increased late systolic shoulder in the radial waveform. Increased late systolic augmentation in the aortic pulse.

Elderly hypertensive

Note: Exaggerated increase in late systolic peak in radial waveform is higher than earlier systolic shoulder, in contrast to young and middle aged hypertensive pulse. This is associated with prominent augmentation of late systolic aortic pulse. Note also the relative reduction in pressure during the diastolic phase indicating reduced coronary artery perfusion pressure.
Pulse Wave Velocity
PWV = Distance (D) / Time delay (ΔT) m/sec

Usually measured over 10 heart beats.
R-wave of ECG used as a timing reference

Carotid Doppler waveform

Femoral Doppler waveform

\[ \text{PWV} = \frac{L}{\Delta T} \]

PWV = Pulse Wave Velocity (m/s)

L = Length between measurement sites (mm)

\[ \Delta T = \text{Transit Time (time delay)} \text{ (ms)} \]
Site A - CAROTID

Site B - RADIAL

<table>
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<th>MeanT (ms)</th>
<th>SD (ms)</th>
<th>N</th>
<th>HR (bpm)</th>
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<td>CAR-RAD</td>
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Pulse Wave Velocity (m/s) 8.6 ± 0.3
The Compliant Vessel vs the Noncompliant Vessel

Compliant
Systole Diastole

Noncompliant
Systole Diastole

Constant Stroke Volume

Aorta

Pulse Pressure

Modified from Kelly R. Circulation. 1989;80:1652-1659. Modified from
Factors influencing PWV
Blood Pressure

- Controls
- Patients with cardiovascular diseases

Aortic pulse wave velocity (m/s) vs. Pulse pressure (mmHg)
Caffeine Increases Aortic Stiffness in Hypertensive Patients

- Systolic Pressure
  - Caffeine: P=0.005
  - Placebo

- Pulse Pressure
  - Caffeine: P<0.01
  - Placebo

- Diastolic Pressure
  - Caffeine: P=NS
  - Placebo

- Pulse Wave Velocity
  - Caffeine: P<0.05
  - Placebo
Acute Effect of Caffeine on Aortic Stiffness in Healthy Subjects
Cigar Smoking Has an Acute Detrimental Effect on Arterial Stiffness

- **Systolic Pressure Response**
  - Aortic vs. Radial comparison
  - P<0.05

- **Augmentation Index Response**
  - P<0.05

- **Diastolic Pressure Response**
  - Aortic vs. Radial comparison
  - P=NS

- **Pulse Wave Velocity Response**
  - P=0.001

- **Pulse Pressure Response**
  - Aortic vs. Radial comparison
  - P<0.05
Alterations of PWV
Dyslipidemia

Systemic arterial compliance \[\log(\text{SAC})\] versus fasting serum high-density (HDL) and low-density (LDL) lipoprotein cholesterol levels for newly diagnosed coronary artery disease cases (■) and matched controls (□). (Adapted from Cameron et al. [64].)
End Stage Renal Disease

Aortic (carotido-femoral)
Upper limb (carotid-radial)
Lower limb (femoro-tibial)

Pulse wave velocity (m/s)

Controls
End-stage renal disease
The role of arterial stiffness as the major cause of cardio-vascular risk can be seen in recent outcome data.

Pulse Wave Velocity

Aortic pulse wave velocity on entry was used to stratify arterial stiffness in a cohort of ESRD patients into tertiles.

1st tertile has almost normal results; 3rd tertile has 6x risk of "all cause' mortality

Arterial Stiffness & Outcomes

Probability of survival (all-cause mortality) in ESRD - London et al
Central Pulse Augmentation (Alx)

- Central pressure Alx on entry was used to stratify arterial stiffness in the cohort of ESRD patients into quartiles.
- 1st quartile has normal results; 4th quartile has 8x risk of “all cause’ mortality.
- CONCLUSION: No other CV risk marker comes close in ESRD to the power of arterial stiffness.

Figure 2. Probability of CV and overall survival of the study population according to the level of Alx divided into quartiles. Log-rank test for overall mortality: \( \chi^2 = 34.02, P < 0.0001 \). Log-rank test for CV mortality: \( \chi^2 = 23.11, P < 0.0001 \).
PWV according to Dialysis in ESRD
Can Pulse Wave Velocity Predict Severity of Coronary Artery Disease?
Number of diseased vessel

PWV (m/sec)

Single  Multiple

P<0.05

ACC/AHA lesion type

A/B1  B2/C

PWV (m/s²)

P<0.05
Relationship between PWV and degree of stenosis

Modified stenosis score system

\[ Y = -7.726 + 1.422 \times X \]

\[ r = 0.550, \ p < 0.0001 \]
Increased Arterial Stiffness in Patients with Cardiac Syndrome X

P < 0.05
Cerebrovascular Disease

Aortic distensibility (dimensionless)

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<th>Controls</th>
<th>Stroke</th>
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<tbody>
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<td>4.9</td>
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Aortic PWV (m/s)

<table>
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<tr>
<th></th>
<th>Controls</th>
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<tbody>
<tr>
<td>9.4</td>
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<td>13.8</td>
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***  **  **
Anti-Hypertensive Drug

Short term medication < 28 d

Long term medication > 28 d

Changes in PWV (m/s)

**A**
- Placebo
- Calcium antagonist
- ACE-inhibitors

**B**
- Placebo
- Calcium antagonist
- Diuretics
- Beta-blockers
- ACE-inhibitors

$p = 0.053$
Effect of Angiotensin II Receptor Blockade on Arterial Stiffness: Beyond Blood Pressure Reduction
결론

Augmentation index, pulse wave velocity를 이용한 arterial stiffness의 측정은 여러 혈관 질환에서 병의 경과를 예측하고 치료 효과를 판단하는 중요한 변수로 인정되고 있으며, 측정 방법의 간편성, 다양한 측정 기계의 개발에 힘입어 앞으로 많은 이용이 예상된다.