Arterial Stiffness: pathophysiology and clinical impact

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Determinants of vascular overload (afterload) on the heart

- Peripheral Resistance
- Arterial Stiffness
- Wave reflection
- Inertance
Arterial Impedance as a determinant of afterload Gradients

\[ \text{PWV} = \frac{Z_c}{Z_c - Z_r} \]

- **Zc**: Characteristic impedance
- **Zr**: Peripheral resistance

Reflection Coefficient:
\[ \text{Reflection Coefficient} = \frac{Z_r - Z_c}{Z_r - Z_c} \]

Zc-characteristic impedance
Zr-peripheral resistance
Mean BP: Cardiac output and peripheral resistance

Systolic pressure

Pulse pressure: ventricular ejection, arterial stiffness, wave reflection

Diastolic pressure
Flow-Pressure relationship - influence of the frequency
(Resistance = slope of the relationship)

\[ R = 8\eta \frac{L}{\pi r^4} \]

(\(\eta\) - viscosity; \(L\) - length; \(r\) - radius - number of vessels)

\[ R = \text{Mean Blood Pressure/Cardiac output} \]
Pressure-flow relationship - influence of the frequency
(Resistance = slope of the relationship)
Diagrammatic representation of volume-pressure relationship

\[ \Delta V/\Delta P = \text{Compliance} \]

\[ \Delta P/\Delta V = \text{Elastance (Stiffness)} \]
Diagrammatic representation of volume-pressure relationship

\[ \Delta V/\Delta P = \text{Compliance} \]

\[ \Delta P/\Delta V = \text{Elastance (Stiffness)} \]

Transition zone
The arterial wall is a heterogeneous material

- Distensible balloon (rubber = elastin)
- Rigid/stiff net (steel = collagen)
- Ballon souple
- Filet inextensible

A. Tedgui and B. Levy, 1994
The arterial wall is a heterogeneous material

A.Tedgui and B. Levy, 1994
Diagrammatic representation of pressure-volume relationships

Pressure

Volume

dP/dV

Einc=1

Einc=2
Arterial function and blood pressure

Pure Conduit Function

Conduit and Cushioning Function

Blood pressure

Systole  Diastole

Mean pressure

Systole  Diastole
Relationship of Resistance (R) and Compliance (C) with diastolic pressure decay

\[ \tau = R.C \]

\[ \alpha = \frac{1}{\tau} = \frac{1}{R.C} \]

* log scale

- \( \tau \): time constant of diastolic decay
- \( \alpha \): slope of diastolic decay

Adapted from Simon et al. Am J Physiol 1979
The diameter-pressure curve

Diameter (mm)

Time (sec)

Local pressure

Diameter (mm)

High-definition echotracking devices
- Wall Track system
- NIUS system

Aplanation Tonometry
- Millar Instruments
Pressure-diameter relationship: a thermodynamic analysis

Viscosity = Dissipated energy

Distensibility = Exchanged energy
Pressure/arterial luminal cross-sectional area and hysteresis loop in vivo before and after desendothelisation

Carotid-femoral pulse wave velocity

\[ \Delta t \]

\[ PWV = \frac{L}{\Delta t} \]

\[ PWV^2 = E_{inc} \cdot IMT_{th}/\rho D \]
Correlation between common carotid artery (CCA) distensibility and aortic pulse wave velocity (PWV) in human population

\[ r = -0.825 \]

\[ p < 0.0001 \]
Pressure wave analysis

- measured pressure wave
- forward/incident pressure wave
- reflected pressure wave
- pulse wave velocity

Young subjects

Old subjects
Effect of arterial stiffness on timing of forward and reflected Waves

PWV 8 m/sec

PWV 12 m/sec

Systolic Augmentation Pressure (Aix)

T - traveling time of pressure wave to reflecting sites and back
Aortic versus Peripheral pulse pressure

Forward-traveling wave
Backward-traveling reflected wave
Actual (composite) wave

T - traveling time of pressure wave to reflecting sites and back
Pressure Waves Recorded Along the Arterial Tree

Aortic (carotid) pressure waveform

ΔP = augmented pressure
PP = pulse pressure
Augmentation index = ΔP / PP
Tsh = time to shoulder
LVET = left ventricular ejection time

Diagram:
- ΔP
- PP
- Tsh
- LVET
- Forward-wave
- Reflected wave
- Actual wave
Relationship between the time of appearance of reflected wave on the pressure wave in central artery (time to shoulder - TSh) and aortic pulse wave velocity (PWV)

R = -0.671
p < 0.0001
Relationship between the time of appearance of reflected wave on the pressure wave in central artery (time to shoulder - TSh) and body height

R = 0.585
p < 0.0001
Arterial Impedance Gradients

Zc-characteristic impedance; Zr-peripheral resistance

Reflection Coefficient \( \Gamma = \frac{Z_R - Z_C}{Z_R + Z_C} = \frac{P_b}{P_f} \)

\[
P_WV = 6 \text{ m/s} \quad P_WV = 10 \text{ m/s} \\
P_WV = 12 \text{ m/s} \quad P_WV = 11 \text{ m/s}
\]

Aorta  Muscular arteries  Resistance vessels
Pressure = 0 + P1 + P2 + P3... = a1 \cos(\omega t + \phi_1) + a2 \cos(\omega t + \phi_2) + a3 \cos(\omega t + \phi_3)...

Fourier series - the mean term and first 6 harmonics of a pressure wave from ascending aorta (Westerhof et al 1979)
Pressure and flow waves broken down into mean term and Fourier series

Modulus is the amplitude of pressure harmonic divided by the amplitude of corresponding flow harmonic, and phase as the delay between corresponding harmonics.
Modulus and phase of impedance in the ascending aorta

McDonald blood flow in the arteries 1994
Schematic representation of vascular impedance (Modulus = Pressure/flow)

- **Peripheral resistance (Zr)**
- **First minimum of impedance modulus - $f_{\text{min}}$** (lowest pressure for a given flow)
- **Characteristic impedance**

![Graph showing vascular impedance with Modulus (dynes sec cm$^{-5}$) on the y-axis and Frequency (Hertz) on the x-axis.]
Pressure and flow waves along the tubular model completely occluded. At the closed end the pressure is maximal and flow zero. The best coupling minimal pressure for maximal flow is at 1/4 of the wavelength (\( \lambda = \text{PWV}/\text{frequency} \)) equal to the distance \( L \) to site of reflection.

\[ L = \frac{\lambda}{4} = \frac{\text{PWV}}{4f} \]

**Example:**
\( \Delta t_p = 0.125 \text{s}, \ 2 \Delta t_p = 0.25 \text{s}, \ f_{\text{min}} = 1/0.25 = 4 \text{Hz} \)
Relationship between the first minimum of impedance modulus and body height

London GM personal data

\[ r = -0.546 \]

\[ P < 0.0001 \]
Relationship between the first minimum of impedance modulus and aortic PWV

$r = 0.495$

$P < 0.0001$

London GM personal data
Schematic representation of vascular impedance (Modulus = Pressure/flow)

Modulus (dynes sec cm⁻⁵)

Z_r = Z_r

Control

ESRD

Frequency (Hertz)

0 1 2 3 4 5 6 7

(Heart rate)

Z_c

f_{min}

f_{min}

Z_c
Representation of the impedance modulus and amplitude (power) of flow harmonics

First minimum of impedance modulus

Flow (ml/m) for different frequencies

(1st = Heart rate)

Cycles (multiples of 1st in Hertz)
Impedance modulus and flow harmonics during exercise (shift of flow harmonics with increased heart frequency)
Heart rate - 200 (3.3Hz)
1st minimum of impedance is close to heart rate (i.e. frequency of the highest flow harmonic for lowest pressure harmonic)

Rabbit

Heart rate - 60 (1Hz)
heart rate is far from 1st min. of impedance
(flow develops a high pressure)

Man
Relationship between the first minimum of impedance modulus and heart period

London GM personal data
Relationship between the ratio of the first minimum of impedance modulus and heart period and body height (better coupling between heart rate and arterial properties in tall subjects)

\[ R = -0.280 \]
\[ P < 0.0001 \]

London GM personal data
Correlation between Fmin/heart frequency and Left Ventricular velocity of fiber shortening

Graph showing a scatter plot with the correlation coefficient $r = -0.338$, $P < 0.001$.

London GM personal data
Diagrammatic representation of the effects of arterial degeneration (right) on aortic systolic pressure time index (orange area) and aortic diastolic pressure time index (yellow area)

O'Rourke M.F: The arterial pulse, Lea Fibiger, 1992
Superimposed simultaneous phasic recording of aortic (Ao), left ventricular (LV) pressures and coronary blood flow (CBF) (Buckeberg et al. Circ Res. 1972)
DPTI/SPTI plotted against Left Ventricular flow distribution between endocardium and epicardium

Adapted from Buckberg et al 1972
Correlation between left ventricular mass and aortic pulse wave velocity

Correlation coefficient: $r = 0.52$

$p < 0.001$

London et al KI 1989
Aortic stiffness and all-cause mortality in general population
(Laurent et al Hypertension 2001)

Kaplan-Meier  P<0.0001
Wave reflection (Aix) and cardiovascular survival

- Log rank test for cardiovascular mortality. Chi square = 23.11; P < 0.0001.
Distribution of Hypertension Subtype in the untreated Hypertensive Population in NHANES III by Age

ISH (SBP ≥ 140 mm Hg and DBP < 90 mm Hg)
SDH (SBP ≥ 140 mm Hg and DBP ≥ 90 mm Hg)
IDH (SBP < 140 mm Hg and DBP ≥ 90 mm Hg)

Frequency of hypertension subtypes in all untreated hypertensives (%)

Numbers at top of bars represent the overall percentage distribution of untreated hypertension by age.
Evolution of Untreated Systolic and Diastolic BP: The Framingham Heart Study

n=2036

Adapted from Franklin et al. Circulation 1997;96:308.
Cardiovascular Risk Associated with Increasing SBP at Fixed Values of DBP

- Two-year risk adjusted for active treatment, sex, age, previous CV complications, and smoking by multiple Cox regression.

Correlation between arterial pulse pressure, wave reflexion (Augmentation index) aortic pulse wave velocity and stroke volume (n=230)

Adapted from London et al KI 1996
Pulse wave analysis:
Definition of waveform landmarks, AI, and characteristic impedance

Arterial Pressure Waves Recorded in Young Subjects

Normotensive Subjects

Pseudo-Hypertension

Essential Hypertension

BRACHIAL BLOOD PRESSURES at 1 year

AORTIC SBP (At 1 year)

Δ SBP (mmHg)

-22.5

-8.0

Per/Ind (n=65)

Aténolol (n=65)

p<0.001

p<0.001

AORTIC PP (At 1 year)

Δ PP (mmHg)

Per/Ind (n=65)  Aténolol (n=65)

-9.3

2.3

p<0.001

p<0.001*

NS

Δ PWV (m/s)

PWV (carotido-femoral)

Per/Ind

atenolol

\[-0.79\]

\[-0.99\]

p<0.001

p<0.001

NS*

AUGMENTATION INDEX (aortic)

Δ AIX (%)

-3.06 (Per/Ind) p=0.002
1.83 (atenolol) p<0.001*

LEFT VENTRICULAR HYPERTROPHY

\[ \Delta \text{LVH (g/m}^2\text{)} \]

\[ \text{Per/Ind} \quad p<0.001 \quad \text{Aténolol} \quad p=0.012 \]

Arterial Impedance Gradients

$Z_c$ - characteristic impedance; $Z_r$ - peripheral resistance

Reflection Coefficient $\left( \Gamma \right) = \frac{Z_r - Z_c}{Z_r - Z_c}$

$Z_c$  $P_b$  $P_f$  $Z_R$  $P_t$

- PWV = 6 m/s
- PWV = 10 m/s
- PWV = 12 m/s
- PWV = 11 m/s

Aorta  Muscular arteries  Resistance vessels