Assessment of Arterials Functions: Is Pulse Wave Velocity ready for Prime Time

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The causes of Cardiovascular Diseases in CKD

- Arteriosclerosis
- Atherosclerosis

- CORONARY ARTERY DISEASE
  - Systolic BP; Diastolic BP
  - Adaptive LVH
  - Maladaptive LVH
  - Systolic/diastolic dysfunction
  - Heart Failure
  - Sudden Death

- CEREBROVASCULAR PERIPHERAL ARTERY DISEASE
  - Volume Overload
  - Hgb; AVF; Na+

*(Decreased coronary perfusion)
*(Decreased coronary reserve)
Atherosclerosis

Arteriosclerosis
Arterial system as « conduit »

Blood transfer

Arterial system as « hydraulic filter »

Cyclic high and pulsatile pressure

Continuous low pressure

Microcirculation capillaries

Cyclic highly pulsatile flow

Continuous flow and perfusion

Aorta
Large arteries mechanics

Artery as a conduit

- Diameter
  - Conduction
    - Kinetic Energy expenditure

Artery as a « hydraulic filter »

- Stiffness
  - Transduction
    - Potential Energy storage

- Wall viscosity
  - Transmission
    - Potential Energy dissipation

Energetic balance of heart-vessel coupling
Threshold

Decades
Years-Months
Months-Days

healthy
subclinical
symptomatic

Intima
Media
Lumen
Plaque
Thrombus

Normal Early Lipid rich Internal rupture Calcified shell Calcified plaque Vulnerable Rupture Thrombus Myocardial infarction Stable

Inflammation and calcification
Scar development with calcification
# Prevalence of discrete plaques on common carotid artery in control subjects and ESRD patients

|                  | Controls | ESRD |  
|------------------|----------|------|-----
| Age (years)      | 48.5 ± 16| 51 ± 16| NS |
| Plaques (%)      | 17.8%    | 56.3%| < 0.01 |
| Type of plaques  |          |      |     |
| • Calcified      | 23.1%    | 91.5%| < 0.01 |
| • Soft/mixed     | 77%      | 9%   | < 0.01 |

London et al Sem Dial 1999
Carotid artery calcifications:
(longitudinal incidence)
Carotid artery calcifications:
(tranversal incidence)
Kono K et al. Composition of plaque patter of coronary culprit lesion in CKD KI 2012;82:344-51

Green-fibrous
Yellow-fatty
Red-necrotic
White-calcified
NC/DC – necrotic core/dense calcium
SAP – stable ang.pect

Kono K et al. KI 2012;82:344-51
Conclusions: Symptomatic plaques are less calcified and more inflamed than asymptomatic plaques. Regardless of clinical outcome, a strong inverse correlation was found between the extent of carotid plaque calcification and the intensity of plaque fibrous cap inflammation as determined by the degree of macrophage infiltration. Carotid plaque calcification is associated with plaque stability, and is a potential spiral CT in vivo quantitative marker for cerebrovascular ischemic event risk. (J Vasc Surg 2004;40:262-9.)
Mechanical Response of a Calcified Plaque Model to Fluid Shear Force

Tiantian C. Lin,¹ Yin Tintut,² Althea Lyman,¹ Wendy Mack,³ Linda L. Demer,⁴ and Tzung K. Hsiai¹

FIGURE 5. Lumped average percentages of nodules remaining attached for both control (triangles) and BGP-treated (squares) cultures (n = 9, p = 0.47) as a function of shear stress (dyn/cm²).

Ankle-Arm Index as a Predictor of Cardiovascular Disease and Mortality in the Cardiovascular Health Study

Newman AB et al for the Cardiovascular Health Study Collaborative Research Group


Kaplan-Meier survival for 1446 CHS participants with prevalent CVD, by categories of AAI level
Brachial systolic blood pressure (mmHg)

Ankle systolic blood pressure (mmHg)

- Ankle-Arm index >0.9
- Ankle-Arm index <0.9

R=0.95
P<0.00001

R=0.61
P<0.01

G.M London personal data
Cushioning function of arterial system: Arterial system as « hydraulic filter »
Diagrammatic representation of pressure-volume relationships

Pressure vs. Volume

Einc=2

Einc=1

dP/dV
ARTERIAL FUNCTION AND

Pure Conduit Function  Conduit and Cushioning Function

Blood pressure

Systole  Diastole  Mean pressure

Blood pressure

Systole  Diastole  Mean pressure
Oxygen Limitation Model

Blood Velocity (NOT capillary recruitment) → Capillary Transit Time → O₂ Extraction → Smaller Fraction of O₂ Available for Metabolism

Normally 2-3 seconds
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)

\[ R = -0.671 \]
\[ p < 0.0001 \]

London et al Hypertension 1992
The time interval of pressure wave to and back from reflection sites

Forward and backward pressures are in phase: no time interval
Pressure wave analysis

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

Young subjects

Old subjects
Role of increased central aortic and pulse pressures in the increase of cardiovascular events

- Decreased Coronary Artery Perfusion Pressure in Diastole ➔ increased risk of MI
- Increase in left ventricular load (LV load) accelerates increase in LV mass ➔ increased risk of LV hypertrophy
- Increase in the central pulse pressure that drives cerebral blood flow ➔ increased stroke risk ➔ Increase chronic kidney disease.

Decreased Coronary Artery Perfusion Pressure in Diastole ➔ increased risk of MI
Correlation between aortic calcification score and aortic PWV in ESRD patients

Pannier et al. Artery 2007
Correlation between age and arterial calcium (Ca) concentration in the aorta and internal iliac artery in nonuremic control subjects

3D plot showing the interaction of PWV and age in relation to the global composite cognitive score for the extended regression model.
Correlation Between CCr (C-G formula) and Aortic PWV

![Graph showing the correlation between Creatinine clearance (mL/min/m²) and Aortic PWV (m/s). The correlation coefficient is \( r = -0.30 \) and the p-value is less than 0.0001. The graph is from Bortolotto et al KI 2001.]
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)

\[ R = -0.671 \]
\[ p < 0.0001 \]

London et al. Hypertension 1992
Follow-up (months)

CV Survival

Aortic PWV

\[ \chi^2 = 72.8 \]
\[ P < 0.00001 \]

<9.7 m/s

>9.7 m/s

>12 m/s

Brachial PWV

\[ \chi^2 = 1.78 \]
\[ P = 0.411 \]

Femoral PWV

\[ \chi^2 = 2.34 \]
\[ P = 0.310 \]

1st tertile

2nd tertile

3rd tertile

Pannier et al. Hypertension 2005
Carotid tonometry

Application of the probe with light pressure on the best palpated pulse.
Probe orthogonal to the long axis of the CCA
Calibration on MBP and DBP of the RA measure
Holding the probe like a pen, do not smash the gel pad, apply as little Pressure as possible
Common carotid artery IMT, diameter and stiffness: Walltrack system ®

Spatial resolution:
- 2D: 200-400 µm
- TM: < 1 µm
- RF Signal: 20-40 µm
Recent developments in echotracking techniques (Pie-Medical Art.Lab®)
Recent developments in echotracking techniques (Pie-Medical Art.Lab ®)
Artlab system: real time, 128 lines RF

X128 RF
IMT ± 17 µm
Diam ± 35 µm
Walltrack system: measurement of flow profiles
Circulation parameters

- Vessel wall
  Diameter wa: 44.83
  Duct wa: 99
  Rise time we: 91
  RR interval we: 0

- Velocity
  Max: 906
  Mean: 209
  Rise time we: 80

- Shear rate
  Min: 220
  Max: 1969
  Max-Min: 1739
  Mean: 408
  Peak-Peak: 897

- Misc
  DC 1e-3 1/kPa: 0.004892
  CC 1e-3 1e-3 kPa: 0.072205

Action
Mechanical stresses in the blood vessel

Circumferential wall stress: \( \sigma \theta = \frac{P \times R}{h} \)

Fluid shear stress: \( \tau = \frac{4 \mu Q}{\pi R^3} \)
Arterial remodeling associated with CKD progression

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean ± SD</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Large arteries</td>
<td></td>
<td></td>
</tr>
<tr>
<td>carotid-femoral pulse wave velocity (m/s)</td>
<td>−0.01 ± 0.04</td>
<td>0.89</td>
</tr>
<tr>
<td>augmentation index (%)</td>
<td>−0.8 ± 0.4</td>
<td>0.045</td>
</tr>
<tr>
<td>carotid systolic BP (mmHg)</td>
<td>−0.5 ± 0.7</td>
<td>0.50</td>
</tr>
<tr>
<td>carotid diastolic BP (mmHg)</td>
<td>−0.8 ± 0.3</td>
<td>0.01</td>
</tr>
<tr>
<td>carotid pulse pressure (mmHg)</td>
<td>0.47 ± 0.52</td>
<td>0.37</td>
</tr>
<tr>
<td>carotid intima-media thickness (µm)</td>
<td>−22 ± 4</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>carotid wall cross-sectional area (mm²)</td>
<td>−0.39 ± 0.09</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>carotid external diastolic diameter (mm)</td>
<td>0.039 ± 0.014</td>
<td>0.006</td>
</tr>
<tr>
<td>carotid internal diastolic diameter (mm)</td>
<td>0.083 ± 0.015</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>carotid wall to lumen ratio (%)</td>
<td>−1.1 ± 0.2</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>carotid stiffness (m/s)</td>
<td>0.28 ± 0.05</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>carotid Young’s elastic modulus (kPa)</td>
<td>59.9 ± 9.9</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>carotid circumferential wall stress (kPa)</td>
<td>2.08 ± 0.43</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Circumf. wall stress = Pressure x Radius
Thicknes
Calcification score: cut-off 390; sensitivity 83%; specificity 69%; PPV 41%; NPV 94%
Aortic PWV: cut-off 10.75 m/s; sensitivity 84%; specificity 73%; PPV 72%; NPV 93%