Ventricular-arterial coupling –
clinical tools and diagnostic indications

Professor Alan G Fraser
Wales Heart Research Institute
Cardiff University, U.K.

Support for research from Hitachi Aloka, & GE Ultrasound
Ventricular–arterial coupling

- Ventricular and aortic elastances
- Local arterial stiffness
- Central aortic pressure
- Aortic pulse wave velocity
- Wave intensity, energy, and reflections
- Aortic wall motion and deformation
  - velocity & timing of systolic expansion
  - speckle tracking
Left ventricular pressure-volume loop

- Pressure
- ESP
- DP
- ESV
- EDV
- Volume

End-systolic pressure-volume relationship $\equiv$ contractility

Isovolumic contraction

Isovolumic relaxation

Ejection

Filling

End-diastolic pressure-volume relationship
The “traditional” concept of ventricular-arterial coupling (Sunagawa)

Elastance = change in pressure for a given change in volume
Myocardial contractility in the left ventricle is inversely related to arterial compliance

Kawaguchi M et al, Circulation 2003; 107: 714-20
Elastance

Change in pressure for a unit change in volume (mmHg/ml)

- **Arterial elastance**
  
  \[ E_A = \frac{ESP}{SV} \] (SV stroke volume)

  Higher elastance = greater sensitivity to volume change, more variable pressure

- **Ventricular elastance** (Ees)
  
  \[ E_{LV} = \frac{ESP}{ESV} \] (ESV LV end-systolic volume)

  Net arterial load exerted on the ventricle
Ventricular-arterial coupling – ratio of elastances

\[ \text{VAC} = \frac{E_A}{E_{LV}} \] with volumes indexed for body surface area

- Greatest efficiency when elastances are matched
- Optimal transfer of blood from LV to aorta
- BP, LV pressure, and CO are maintained in a physiological range
- Normal ratio \( \sim 1.0 \pm 0.36 \)
- Normal \( E_A \) \( 2.2 \pm 0.8 \) mmHg / ml
- Normal \( E_{LV} \) \( 2.3 \pm 1.0 \) mmHg / ml

*Chantler PD et al, J Appl Physiol 2008;105:1342-51*
Ventricular-arterial coupling – example

\[
VAC = \frac{E_A}{E_{LV}}
\]

\[
= \frac{ESP}{SV} \div \frac{ESP}{ESV}
\]

\[
= \frac{ESP}{SV} \times \frac{1}{ESP/ESV}
\]

\[
= \frac{ESP}{SV} \times \frac{ESV}{ESP}
\]

\[
\frac{ESP}{SV} \times \frac{ESV}{ESP}
\]

\[
= ESV \div SV
\]
M aged 30, triathlete

SV = 49 ml
VAC = ESV / SV
= 41 / 49 = 0.84
Combined Ventricular Systolic and Arterial Stiffening in Patients With Heart Failure and Preserved Ejection Fraction

Implications for Systolic and Diastolic Reserve Limitations

Miho Kawaguchi, MD; Ilan Hay, MD; Barry Fetics, MSE; David A. Kass, MD

Circulation 2003; 107: 714-20

also – Margulescu A et al, Am J Cardiol 2012 (e-pub)
Imaging arterial stiffness

• **BETA INDEX**
  - Stiffness
  - Adjusted for BP
  - No units

\[ \beta = \frac{\log_n \left( \frac{P_s}{P_d} \right)}{(D_s - D_d / D_d)} \]

• **EPSILON**
  - Peterson’s pressure-strain elastic modulus
  - Measured in kPa

\[ E_p = \frac{(P_s - P_d) D_d}{(D_s - D_d)} \]
Normative values of conduit arterial function
Influence of gender, age, and body mass index

\( \beta \), men (n 1,148)

\( \beta \), women (n 926)

ETIC  E-Tracking International Collaboration
2,074 healthy subjects aged 3-85 years
Central arterial pressure changes with age

Central pressure augmentation

Peripheral pressure amplification

McDonald's Blood Flow in Arteries
“Direct” estimation of central arterial pressure
Principles of aplanation tonometry

Diameter is scaled to systolic and diastolic pressure

Assumed that diameter and pressure are linearly related
Aplanation tonometry of a peripheral artery (radial)
Pulse wave analysis with “transfer function”
Impact of arterial load (AI) on LV function (n=303)
Non-invasive estimation of pulse wave velocity

$\text{PWV} = \frac{\text{transit time}}{\text{distance (brachial – femoral)}}$

- Sphygmocor – sequential
- Complior – simultaneous
- Vicorder – cuffs
Reference values for pulse wave velocity

\[ n = 11,092 \]
Prognostic utility of aortic pulse wave velocity

PWV added independent prognostic value to the standard Framingham risk score

Mitchell GF et al, Circulation 2010; 1221: 505-11
Wall tracking of common carotid artery

Diameter / distension waveform, calibrated as estimate of pressure

Simultaneous measurement of blood velocity at same site

→ Non-invasive wave intensity
Arterial wave intensity

There are 4 types of waves = \( U \) \( P \)

- Forward compression \( \uparrow \) \( \uparrow \)
- Forward expansion \( \downarrow \) \( \downarrow \)
- Backward compression \( \downarrow \) \( \uparrow \)
- Backward expansion \( \uparrow \) \( \downarrow \)

The time integral of wave intensity is energy
The major “determinant” of reflected wave energy is left ventricular systolic function

$n = 106, 57 M, aged 46 \pm 12 (22-71) years$

$r = 0.81, p<0.0001$

$\log_n FCW$ integral

from wave intensity studies

$\log_n BCW$ integral

$M$ FOR $E$
Calculation of wave speed

Early systolic slope of pressure / velocity loop

Wave speed
\[ c = \frac{dP}{dU}/\rho \]

Harada A et al, Heart Vessels 2002; 17: 61
Comparison of antihypertensive drugs (ASCOT)
Difference in the magnitude of mid-systolic reflections

\[ \Delta \text{ wave reflection index} = 3.5\% \]

Manisty C et al, Hypertension 2009; 54: 724-30
Wave Reflection Predicts Cardiovascular Events in Hypertensive Individuals Independent of Blood Pressure and Other Cardiovascular Risk Factors

An ASCOT (Anglo-Scandinavian Cardiac Outcome Trial) Substudy

259 subjects followed for mean of 5.9 years

<table>
<thead>
<tr>
<th>Predictors of Cardiovascular Events</th>
<th>Beta Coefficient</th>
<th>SE</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Log WRI</td>
<td>2.17</td>
<td>0.03</td>
<td></td>
</tr>
<tr>
<td>DBP, mm Hg</td>
<td>0.94</td>
<td>0.01</td>
<td></td>
</tr>
<tr>
<td>Carotid PP, mm Hg</td>
<td>1.01</td>
<td>0.2</td>
<td></td>
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</tbody>
</table>

Model to predict LVMI

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Beta Coefficient</th>
<th>SE</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Log WRI*</td>
<td>6.6</td>
<td>3.2</td>
<td>0.04</td>
</tr>
<tr>
<td>Log WRI† (fully adjusted)</td>
<td>7.3</td>
<td>3.3</td>
<td>0.03</td>
</tr>
<tr>
<td>P_b/P_r*</td>
<td>10.0</td>
<td>8.9</td>
<td>0.3</td>
</tr>
<tr>
<td>P_b/P_r† (fully adjusted)</td>
<td>14.7</td>
<td>10.7</td>
<td>0.2</td>
</tr>
<tr>
<td>cAl_x*</td>
<td>0.1</td>
<td>0.1</td>
<td>0.4</td>
</tr>
<tr>
<td>cAl_x† (fully adjusted)</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
</tr>
<tr>
<td>Carotid wavespeed*</td>
<td>0.8</td>
<td>0.5</td>
<td>0.1</td>
</tr>
<tr>
<td>Carotid wavespeed† (fully adjusted)</td>
<td>0.7</td>
<td>0.5</td>
<td>0.2</td>
</tr>
</tbody>
</table>
Circumferential myocardial stress during systole

Chirinos JA et al, Circulation 2009; 119: 2798-2807
## Analysis of treatment of hypertension

Prospective open-label study of barnidipine

<table>
<thead>
<tr>
<th></th>
<th>20 well controls</th>
<th>21 untreated hypertensives</th>
<th>After 6 m treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Blood pressure</strong></td>
<td>126 / 78</td>
<td>159 / 96***</td>
<td>138 / 81***</td>
</tr>
<tr>
<td><strong>Augmentation index</strong></td>
<td>13 ± 5</td>
<td>22 ± 7**</td>
<td>17 ± 8**</td>
</tr>
<tr>
<td><strong>Beta index</strong></td>
<td>10 ± 3</td>
<td>11 ± 3</td>
<td>10 ± 3</td>
</tr>
<tr>
<td><strong>Epsilon</strong></td>
<td>126 ± 41</td>
<td>175 ± 49**</td>
<td>155 ± 53**</td>
</tr>
<tr>
<td><strong>Arterial compliance</strong></td>
<td>0.9 ± 0.3</td>
<td>0.6 ± 0.2**</td>
<td>0.7 ± 0.2</td>
</tr>
<tr>
<td><strong>Wave speed</strong></td>
<td>6.8 ± 1.0</td>
<td>7.8 ± 1.0**</td>
<td>7.5 ± 1.7</td>
</tr>
<tr>
<td><strong>Forward pressure</strong></td>
<td>108 ± 7</td>
<td>137 ± 17***</td>
<td>124 ± 14*</td>
</tr>
<tr>
<td><strong>Backward pressure</strong></td>
<td>17 ± 5</td>
<td>21 ± 6*</td>
<td>18 ± 3</td>
</tr>
</tbody>
</table>

* <0.05
** <0.01
*** <0.001

Palombo C, Clin Ther 2009;31:2873-85
Tissue velocity of aortic wall motion
Aortic wall motion in Marfan syndrome
Prospective, double-blind, randomised cross-over

\[ \Delta \text{Time to peak systolic velocity of anterior aortic wall motion (ms)} \]

- Perindopril 4 mg
- Verapamil 240 mg SR
- Atenolol 75 mg

\[ \text{p} = 0.003 \]

Atenolol also reduced heart rate by 16%
so it reduced pulsatile stress

\[ +8\% +11\% \]

Williams A et al, Eur J Clin Invest 2012 (e-pub)
Mechanical deformation of conduit arterial wall

Speckle tracking – “Wave Intensity Wall Analysis”

Radial strain  

Longitudinal strain

Larsson M et al, IEEE Trans Ultrason 2011; 58: 2244-51
also – Bjällmark A et al, Heart Vessels 2011; 26:289-97
Ventriculo-arterial coupling – clinical applications

• Pathophysiological insights from clinical research
  – Mechanisms of ISH, and of LVF in HFNEF
  – Non-uniformity of conduit arterial function

• More accurate diagnosis, better prognosis
  – Pulse wave velocity
  – Mid-systolic wave reflections

• Selecting and monitoring drug treatment
  – to reduce central arterial pressure
  – to delay and reduce mid-systolic reflections
  – to reduce net and pulsatile stress in aorta