Wave Intensity Analysis Provides Novel Insights into Pulmonary Hypertension

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Background
Arterial waves

Proximal artery

Forward compression wave (FCW)

$dP$

$dU$

$P$: pressure
$U$: velocity

Su et al., Acta Physiol, 2016
Arterial waves

Proximal artery

Forward compression wave (FCW)

Forward decompression wave (FDW)

$\uparrow dP$

$\uparrow dU$

$\downarrow dP$

$\downarrow dU$

P: pressure
U: velocity

Flow Direction

Su et al., Acta Physiol, 2016
Arterial waves

Proximal artery

Forward compression wave (FCW)

Forward decompression wave (FDW)

Distal artery

Backward compression wave (BCW)

Backward decompression wave (BDW)

Su et al., Acta Physiol, 2016
Wave intensity analysis (WIA)

- Analysis of the incremental changes in pressure (P) and flow velocity (U) in a circulation

- Wave intensity: energy carried by a wave
  \[ \text{d}I = \text{d}P \times \text{d}U \]  
  (Unit W/m\(^2\) = J/sm\(^2\))
Pulmonary hypertension (PH)

Mean pulmonary arterial pressure (PAPm) ≥ 25 mmHg
→ right heart failure

PAH (Pulmonary arterial hypertension)

CTEPH (Chronic thromboembolic PH)

PH due to left heart disease

PH due to lung disease

PH with unclear or multifactorial causes
WIA in pulmonary artery

- WIA in the pulmonary artery in man is feasible!
- Clinical implications?

Lau et al, Eur Respir J, 2014
Objective

• Assess arterial wave characteristics in the pulmonary artery

• Explore the clinical usefulness of WIA in pulmonary hypertension
Study design
Inclusion criteria

• Patients referred to the cardiac catheterisation laboratory for clinical reasons

• Control subjects: no significant heart or lung disease

• PH patients: patients with confirmed or suspected PAH or CTEPH
Right heart catheterisation

Right heart catheterisation with simultaneous pressure and velocity measurements.
• Data ensemble averaged using the R-wave of ECG
Data processing

- Data ensemble averaged using the R-wave of ECG
- Calculation of wave speed (sum of squares method)

\[
c = \frac{1}{\rho} \cdot \sqrt{\frac{\sum dP^2}{\sum dU^2}}
\]
Data processing

- Data ensemble averaged using the R-wave of ECG
- Calculation of wave speed (sum of squares method)
- Wave intensity (WI) normalized to number of samples in the cardiac cycle

\[ WI = dP \frac{CCD}{dt} \cdot dU \frac{CCD}{dt} \]

*CCD: cardiac cycle duration*
Data processing

- Data ensemble averaged using the R-wave of ECG
- Calculation of wave speed (sum of squares method)
- Wave intensity (WI) normalized to number of samples in the cardiac cycle

- **Separation of forward and backward waves**

\[
Forward: \quad WI_+ = \left( \frac{dP \cdot CCD}{dt} + \rho \cdot c \frac{dU \cdot CCD}{dt} \right) / 4\rho c
\]

\[
Backward: \quad WI_- = -\left( \frac{dP \cdot CCD}{dt} - \rho \cdot c \frac{dU \cdot CCD}{dt} \right) / 4\rho c
\]
Results
Study subjects

Recruited
N = 36

Excluded
N = 5

Control
N = 10
PAPm: 17 mmHg

PAH
N = 11
PAPm: 47 mmHg

CTEPH
N = 10
PAPm: 48 mmHg
WIA pattern

Control
WIA pattern

Control

PAH

FCW

FDW

BCW

WI (10^4 Wm^-2)

Pressure

Velocity

P (mmHg)

U (cm/s)

0 0.2 0.4 0.6 0.8

0 0

0 10 20 30

0 20 40 60

0 20 40 60

W (10^4 Wm^-2)
WIA pattern

CTEPH

PAH

FCW

FDW

BCW

FCW

FDW

BCW
PH patients = PAH + CTEPH

Wave speed

- Mild PH: 25–34 mmHg
- Moderate PH: 35–44 mmHg
- Severe PH: >45 mmHg
Wave reflection

Wave reflection index (WRI) = BCW/FCW
Wave reflection

Impedance mismatch

No significant difference
The right ventricle

FCW energy

No significant difference
The right ventricle

**FCW energy**

Control | PAH | CTEPH

No significant difference

**RV stroke energy**

Control | PAH | CTEPH

No significant difference
The right ventricle

**FCW energy**

*FCW energy (10^3 J m^-2)*

- Control
- PAH
- CTEPH

**FCW to RV energy ratio**

*FCW to RV energy ratio**

- Control
- PAH
- CTEPH

**RV stroke energy**

*RV stroke energy (10^2 J m^-2)*

- Control
- PAH
- CTEPH

*Significant differences indicated by asterisks:* * denotes p < 0.05, ** denotes p < 0.01.
The right ventricle

FCW energy

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>PAH</th>
<th>CTEPH</th>
</tr>
</thead>
<tbody>
<tr>
<td>FCW energy (10³ J·m⁻²)</td>
<td>2</td>
<td>6</td>
<td>4</td>
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</table>

RV stroke energy

<table>
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<th></th>
<th>Control</th>
<th>PAH</th>
<th>CTEPH</th>
</tr>
</thead>
<tbody>
<tr>
<td>RV energy (10² J·m⁻²)</td>
<td>2</td>
<td>4</td>
<td>8</td>
</tr>
</tbody>
</table>

FCW to RV energy ratio

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>PAH</th>
<th>CTEPH</th>
</tr>
</thead>
<tbody>
<tr>
<td>FCW to RV energy ratio</td>
<td>2</td>
<td>10</td>
<td>15</td>
</tr>
</tbody>
</table>

Differentiating CTEPH from PAH (FCW to RV energy ratio)

AUROC = 0.87

p < 0.001
Discussion and conclusion
Early detection of disease

Progressive loss of microcirculation

Vascular damage in > 50% of the microcirculation

Impedance mismatch occurs in the initial phase of disease (as indicated by wave reflection)

Lau et al., Eur Heart J, 2011
PAH versus CTEPH

- **PAH**: pharmacological treatment
- **CTEPH**: pulmonary endarterectomy

- **FCW to RV energy ratio** greater in CTEPH than PAH
  - \( \Rightarrow \) differences in RV function
    - CTEPH: rapid adaptation
    - PAH: gradual adaptation
- May serve as an additional measurement
Conclusion

- **Wave speed** increases in PH ⇒ greater arterial stiffness.
- **Wave reflection** is minimal in individuals without pulmonary vascular disease.
- Large wave reflection in pulmonary hypertension and it is unrelated to severity.
- Increased wave reflection may be an early indicator of pulmonary vascular disease.
- **FCW to RV energy ratio** can differentiate between PAH and CTEPH.
Thank you!
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Right heart catheterisation

Combowires

Sensor

Catheter

Right Heart Catheter
Calculations – wave intensity

“Original” wave intensity \((Wm^{-2})\)

\[
dI = dP \cdot dU
\]

“Time-normalized” Wave intensity \((Wm^{-2}s^{-2})\)

\[
WI = \frac{dP}{dt} \cdot \frac{dU}{dt}
\]

Wave intensity normalized to sample numbers \((Wm^{-2})\)

\[
WI = dP \frac{CCD}{dt} \cdot dU \frac{CCD}{dt}
\]
Calculations – RV energy

**RV stroke work**

\[ RVSW = (PAPm - RAP) \cdot RVSV \]

**RV energy density**

\[
RV energy\ density = \frac{RVSW}{CSA} = \frac{(PAPm - RAP) \cdot RVSV}{RVSV \cdot HR/U_{mean}}
\]

\[
= \frac{(PAPm - RAP)}{HR/U_{mean}}
\]

\[
= (PAPm - RAP) \cdot U_{mean} \cdot CCD
\]
### Participant characteristics

<table>
<thead>
<tr>
<th></th>
<th>Control N = 10</th>
<th>PAH N = 11</th>
<th>CTEPH N = 10</th>
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</thead>
<tbody>
<tr>
<td><strong>Age (yrs)</strong></td>
<td>59 ± 14</td>
<td>56 ± 21</td>
<td>66 ± 9</td>
</tr>
<tr>
<td><strong>Male, n (%)</strong></td>
<td>8 (80 %)</td>
<td>2 (18 %)*</td>
<td>2 (20 %)*</td>
</tr>
<tr>
<td><strong>BMI (kg/m²)</strong></td>
<td>28 ± 5</td>
<td>26 ± 5</td>
<td>27 ± 6</td>
</tr>
<tr>
<td><strong>HR (beats/min)</strong></td>
<td>73 ± 8</td>
<td>81 ± 8</td>
<td>80 ± 15</td>
</tr>
<tr>
<td><strong>PAPm (mmHg)</strong></td>
<td>17 ± 3</td>
<td>47 ± 11*</td>
<td>42 ± 8*</td>
</tr>
<tr>
<td><strong>TPRI (WU/m²)</strong></td>
<td>7 ± 2</td>
<td>25 ± 13*</td>
<td>20 ± 8*</td>
</tr>
<tr>
<td><strong>CI, L/min/m²</strong></td>
<td>2.6 ± 0.5</td>
<td>2.3 ± 1.1</td>
<td>2.4 ± 0.8</td>
</tr>
<tr>
<td><strong>BNP (ng/L)</strong></td>
<td>50 ± 64</td>
<td>522 ± 141*</td>
<td>265 ± 166*</td>
</tr>
</tbody>
</table>

* *p < 0.05 vs control*
Pressure separation

Control

PH

- Black: Measured
- Blue: Forward
- Red: Backward
Wave speed

Compliance:
- ln(compliance) vs. Wave speed (m/s)
  - rho = 0.71, p < 0.01

mPAP:
- mPAP (mmHg) vs. Wave speed (m/s)
  - rho = 0.61, p < 0.01

TAPSE:
- TAPSE (cm) vs. Wave speed (m/s)
  - rho = 0.57, p = 0.01

BNP:
- ln(BNP) vs. Wave speed (m/s)
  - No association
Wave reflection

Compliance

\[ \rho = 0.34, \quad p < 0.16 \]

\[ \rho = -0.10, \quad p < 0.68 \]

\[ \rho = 0.22, \quad p = 0.37 \]

\[ \rho = 0.06, \quad p = 0.81 \]

No association

mPAP

No association

TAPSE

No association

BNP

No association