Longitudinal changes in aortic reservoir function independently predict declining renal function among healthy individuals

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Haemodynamics and renal function

High blood pressure (BP) is associated with poor renal function and vice versa.

Renal function may be more closely related central haemodynamics (including central BP)

- Central BP indices\(^1\) are associated with renal function.

\(^1\)Safar ME et al. Hypertension 2002; 39: 735-738
Reservoir-excess pressure paradigm

**Excess pressure**
- Excess LV work
- Analogous to the flow wave

**Reservoir pressure**
- Input-compliance-resistance to outflow
- Aortic “buffering” capacity

**Physiologically plausible**
- Describe age- and exercise-related changes in central BP (invasive pressure and flow velocity)\(^1,\,2\)
- Theoretical principles supported by in vivo human study\(^3\)

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\(^3\)Schultz et al. ATVB 2014; 34: 1597-603
Reservoir-excess pressure paradigm

Excess pressure
Excess LV work
Analogous to the flow wave

Reservoir pressure
Input-compliance-resistance to outflow
Aortic “buffering” capacity

Clinically relevant
• Cardiovascular events and mortality\textsuperscript{1-4}
• Grey matter atrophy\textsuperscript{5}
• Exercise induced albuminuria\textsuperscript{6}

\textsuperscript{1}Davies JE et al. Hypertension 2014; 64: 60-68
\textsuperscript{3}Narayan et al. Hypertension 2015; 65: 629-35
\textsuperscript{4}Cheng et al. Int J Cardiol 2016; 215: 338-95
\textsuperscript{5}Climie RE et al. Cardiovasc Diabetol 2014; 13: 143
\textsuperscript{6}Climie RE et al. Am J Physiol Heart Circ 2015; 308: H1136-42
To our knowledge no studies have examined the **longitudinal changes in reservoir characteristics** and the association of these changes with **renal function**.
Aim and Hypothesis

AIM
To determine the association between the change in aortic reservoir characteristics and the change in renal function in healthy individuals

HYPOTHESIS
The change in aortic reservoir characteristics will be associated with the change in renal function
Flow of study participants

Powered for exercise haemodynamics

Baseline
(January to December 2011)
n=40

Lost to follow up n=6
Moved interstate n=1

Follow up
(June to November 2014)
n=33
Mean follow up time (3.0±0.3 years)

Exclusion criteria
A clinical history of cardiovascular disease or severe pulmonary disease
Arrhythmia
Pregnancy

Study Protocol

Visit 1

Visit 2

Within in 10 days
Central blood pressure

Radial waveform calibrated with brachial cuff systolic and diastolic BP

Generalised Transfer Function$^1$

Reservoir characteristics

Radial waveforms ensemble averaged

Reservoir pressure derived based on previous equations

Excess pressure = total measured pressure wave – reservoir pressure

Custom Matlab programs

Davies JE et al. Hypertension 2014; 64: 60-68
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<td><strong>Age (years)</strong></td>
<td>54±9</td>
<td>57±9</td>
<td>3±0</td>
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<tr>
<td><strong>Body mass index (kg/m²)</strong></td>
<td>25.3±3.5</td>
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<td><strong>Daytime systolic BP (mmHg)</strong></td>
<td>136±14</td>
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<td><strong>In-clinic systolic BP (mmHg)</strong></td>
<td>115±9</td>
<td>119±13</td>
<td>5±11</td>
<td>0.017</td>
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<td><strong>Current smoker, n (%)</strong></td>
<td>2 (6)</td>
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### Participant Characteristics (n=33)

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<td>4.7±0.4</td>
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<td>Insulin (IU/mL)</td>
<td>2.5±4.7</td>
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<td>6.8±6.1</td>
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<td>eGFR (mL/min/1.73m^2)</td>
<td>107.8±4.0</td>
<td>98.9±3.4</td>
<td>-8.85±2.2</td>
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The change in reservoir characteristics

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<td>Reservoir pressure integral (Pa.s)</td>
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<td>451±104</td>
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<td>Central systolic BP (mmHg)</td>
<td>103±10</td>
<td>108±14</td>
<td>6±10</td>
<td>0.003</td>
</tr>
<tr>
<td>Central pulse pressure (mmHg)</td>
<td>37±5</td>
<td>42±9</td>
<td>5±6</td>
<td>&lt;0.001</td>
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<td>Augmented pressure (mmHg)</td>
<td>8±5</td>
<td>12±7</td>
<td>4±4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Augmentation index (%)</td>
<td>21±11</td>
<td>27±11</td>
<td>6±7</td>
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<td>Aortic PWV (m/s)</td>
<td>6.5±1.4</td>
<td>7.3±1.2</td>
<td>0.9±1.3</td>
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Aim

Association of change in excess pressure and change in renal function

**Independent of age at follow up, change in BMI and ambulatory daytime systolic BP (β =-0.03, p=0.046)**
Association of change in excess pressure and change in renal function

Change in aortic stiffness ≠ change in eGFR

\[ r = 0.15, \ p = 0.42 \]

Independent of hypertension status (ambulatory daytime systolic BP ≥ 135/85 and/or using antihypertensives) \( (\beta = -0.03, \ p = 0.020) \)
Independent of age at follow up, change in BMI, 24 hour daytime systolic BP ($\beta = 140.33$, $p = 0.035$).

No significant interaction ($p > 0.05$ for product term).

The addition of glucose did not alter the relationship between excess pressure and eGFR but it did render it borderline significant ($p = 0.057$).

- Association of change in glucose and change in excess pressure

$r = 0.38$, $p = 0.038$
Potential mechanism of kidney damage

↑ Pressure / Excess pressure

Stiffened aorta

↑ aPWV
Potential mechanism of kidney damage

Excess pressure

Stiffened aorta

Stiffened aorta

aPWV
Conclusions

• First longitudinal pilot data of reservoir characteristics

• Excess pressure is associated with a decline in renal function among healthy people over a 3 year follow up period

  Larger cohort, with more detailed analysis of metabolic and haemodynamic changes is required
Thank you

Diabetes Australia Research Trust

Study participants

ARTERY Society travel grant

Baker IDI

UNIVERSITY of TASMANIA

MENZIES Institute for Medical Research