Biomechanical wall stress and rupture potential in AAA
- Data from the MA³RS Trial -

Barry Doyle PhD, FIEAust

Vascular Engineering Laboratory
Harry Perkins Institute of Medical Research &
School of Engineering, The University of Western Australia
No conflicts of interest to disclose
Big team effort!

Nik Bappoo
Paul Norman
Jordan D’Souza
Simon Duong
Thomas Edland

Luke Falconer
Michael Millett
Quentin Bore
Chloe Dacher
Grand Joldes
Arjun Balaji

Rachael Forsythe
David Newby
Olivia McBride
Marc Dweck
Jenny Robson

Peter Hoskins
Noel Conlisk
Scott Semple
Calum Gray
Tom MacGillivray
What do we currently know about biomechanics-based AAA rupture risk?
Biomechanical Imaging Markers as Predictors of Abdominal Aortic Aneurysm Growth or Rupture: A Systematic Review

R. Indrakusuma a, H. Jalalzadeh a, R.N. Planken b, H.A. Marquering b,c, D.A. Legemate a, M.J.W. Koelemay a, R. Balm a,*

a Department of Surgery, Academic Medical Center, Amsterdam, The Netherlands
b Department of Radiology, Academic Medical Center, Amsterdam, The Netherlands
c Department of Biomedical Engineering and Physics, Academic Medical Center, Amsterdam, The Netherlands

WHAT THIS PAPER ADDS

None of the proposed biomechanical imaging markers are conclusively associated with AAA rupture or growth. Although peak wall stress (PWS), as calculated with finite element analysis (FEA), was significantly higher in ruptured AAAs than in intact AAAs across multiple studies, there was confounding bias between groups because of baseline differences in AAA diameter. In addition, there is conflicting evidence on whether increased wall stress is associated with growth. Furthermore, although FEA is frequently applied in research, the methodology has not been standardised and its technical limitations have only marginally improved.
Our aim

Perform a prospective study to determine if biomechanics-based risk assessment **DOES** or **DOES NOT** predict rupture or the need for surgery

2014-2018
Cohort & imaging

Patients Screened
1942

Ineligible Patients, 1201
AAA diameter <40 mm, 920
Other major illness, 163
Contraindication to scan, 88
Planned surgery, 14
Other, 16

Eligible Patients
741

Non-recruited Eligible Patients, 380
Declined, 288
Unable to contact, 86
Unable to recruit, 6

Consented Patients
361

Withdrawn, 19
Unable to tolerate MRI, 16
Aneurysm too small, 3

Study Population
342

Baseline imaging
 Ultrasound
 CT angiography (CTA)
 MRI

Follow-up every 6 months for 24 months with ultrasound and clinical follow-up for 22 years. The primary endpoint was the composite of aneurysm rupture or repair.

295 included in cohort - blind to outcome

Missing/poor quality images (n = 47)
## Cohort characteristics

<table>
<thead>
<tr>
<th>Case Description</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases</td>
<td>295</td>
</tr>
<tr>
<td>Male [%]</td>
<td>85 %</td>
</tr>
<tr>
<td>Smoker [%]</td>
<td>88 %</td>
</tr>
<tr>
<td>Baseline diameter [mm]</td>
<td>49.6 ± 7.8</td>
</tr>
<tr>
<td>Growth rate [mm/y]</td>
<td>2.9 ± 2.6</td>
</tr>
</tbody>
</table>
Cohort characteristics

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>Stable</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases</td>
<td>295</td>
<td>181</td>
</tr>
<tr>
<td>Male [%]</td>
<td>85 %</td>
<td>84 %</td>
</tr>
<tr>
<td>Smoker [%]</td>
<td>88 %</td>
<td>86 %</td>
</tr>
<tr>
<td>Baseline diameter [mm]</td>
<td>49.6 ± 7.8</td>
<td>47.1 ± 6.6</td>
</tr>
<tr>
<td>Growth rate [mm/y]</td>
<td>2.9 ± 2.6</td>
<td>2.4 ± 2.4</td>
</tr>
</tbody>
</table>
## Cohort characteristics

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>Stable</th>
<th>Repaired</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases</td>
<td>295</td>
<td>181</td>
<td>101</td>
</tr>
<tr>
<td>Male [%]</td>
<td>85 %</td>
<td>84 %</td>
<td>80 %</td>
</tr>
<tr>
<td>Smoker [%]</td>
<td>88 %</td>
<td>86 %</td>
<td>79 %</td>
</tr>
<tr>
<td>Baseline diameter [mm]</td>
<td>49.6 ± 7.8</td>
<td>47.1 ± 6.6</td>
<td>51.7 ± 6.1</td>
</tr>
<tr>
<td>Growth rate [mm/y]</td>
<td>2.9 ± 2.6</td>
<td>2.4 ± 2.4</td>
<td>4.1 ± 2.7</td>
</tr>
</tbody>
</table>
## Cohort characteristics

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>Stable</th>
<th>Repaired</th>
<th>Ruptured</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases</td>
<td>295</td>
<td>181</td>
<td>101</td>
<td>13</td>
</tr>
<tr>
<td>Male [%]</td>
<td>85 %</td>
<td>84 %</td>
<td>80 %</td>
<td>76 %</td>
</tr>
<tr>
<td>Smoker [%]</td>
<td>88 %</td>
<td>86 %</td>
<td>79 %</td>
<td>88 %</td>
</tr>
<tr>
<td>Baseline diameter [mm]</td>
<td>49.6 ± 7.8</td>
<td>47.1 ± 6.6</td>
<td>51.7 ± 6.1</td>
<td>53.6 ± 8.9</td>
</tr>
<tr>
<td>Growth rate [mm/y]</td>
<td>2.9 ± 2.6</td>
<td>2.4 ± 2.4</td>
<td>4.1 ± 2.7</td>
<td>4.6 ± 3.2</td>
</tr>
</tbody>
</table>

Blind to groupings until after biomechanical analyses
Biomechanical assessment at baseline
Patient-specific wall thickness and blood pressure

RPI = \frac{Wall\ Stress}{Wall\ Strength}
Do cases that went on to rupture or need repair have higher biomechanical indices at baseline?
Do cases that went on to rupture or need repair have higher biomechanical indices at baseline?

<table>
<thead>
<tr>
<th></th>
<th>Stable</th>
<th>Repaired/Ruptured</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases [n]</td>
<td>181</td>
<td>114</td>
<td>-</td>
</tr>
<tr>
<td>Rupture Potential Index</td>
<td>0.47 ± 0.25</td>
<td>0.53 ± 0.30</td>
<td>0.0070</td>
</tr>
<tr>
<td>Peak wall stress [MPa]</td>
<td>0.35 ± 0.16</td>
<td>0.36 ± 0.13</td>
<td>0.0979</td>
</tr>
</tbody>
</table>

YES
Cases that later ruptured or needed repair had higher RPI at baseline
Do cases that went on to rupture or need repair have higher biomechanical indices at baseline?

<table>
<thead>
<tr>
<th></th>
<th>Stable</th>
<th>Repaired/Ruptured</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases [n]</td>
<td>181</td>
<td>114</td>
<td>-</td>
</tr>
<tr>
<td>Rupture Potential Index</td>
<td>0.47 ± 0.25</td>
<td>0.53 ± 0.30</td>
<td>0.0070</td>
</tr>
<tr>
<td>Peak wall stress [MPa]</td>
<td>0.35 ± 0.16</td>
<td>0.36 ± 0.13</td>
<td>0.0979</td>
</tr>
<tr>
<td>Baseline diameter [mm]</td>
<td>47.1 ± 6.6</td>
<td>51.9 ± 6.4</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Growth rate [mm/y]</td>
<td>2.40 ± 2.45</td>
<td>4.16 ± 2.79</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

**BUT** diameter was also **larger** and repaired/ruptured cases **expanded faster**
What about smaller cases?
Diameter < 50 mm
What about smaller cases?
Diameter < 50 mm

<table>
<thead>
<tr>
<th></th>
<th>Stable</th>
<th>Repaired/Ruptured</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases [n]</td>
<td>170</td>
<td>39</td>
<td>-</td>
</tr>
<tr>
<td>Rupture Potential Index</td>
<td>0.47 ± 0.26</td>
<td>0.57 ± 0.42</td>
<td>0.0745</td>
</tr>
<tr>
<td>Peak wall stress [MPa]</td>
<td>0.36 ± 0.17</td>
<td>0.36 ± 0.16</td>
<td>0.5699</td>
</tr>
</tbody>
</table>

NO
Small cases that later ruptured or needed repair had similar RPI at baseline
What about smaller cases? Diameter < 50 mm

<table>
<thead>
<tr>
<th></th>
<th>Stable</th>
<th>Repaired/Ruptured</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases [n]</td>
<td>170</td>
<td>39</td>
<td>-</td>
</tr>
<tr>
<td>Rupture Potential Index</td>
<td>0.47 ± 0.26</td>
<td>0.57 ± 0.42</td>
<td>0.0745</td>
</tr>
<tr>
<td>Peak wall stress [MPa]</td>
<td>0.36 ± 0.17</td>
<td>0.36 ± 0.16</td>
<td>0.5699</td>
</tr>
<tr>
<td>Baseline diameter [mm]</td>
<td>44.6 ± 3.78</td>
<td>46.3 ± 3.01</td>
<td>0.0010</td>
</tr>
<tr>
<td>Growth rate [mm/y]</td>
<td>2.35 ± 2.43</td>
<td>4.37 ± 2.48</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Diameter was still **larger** and repaired/ruptured cases **expanded faster**.
If we risk factor-match the small (<50 mm) cases
Matched for diameter, gender and AAA history ➔ Gender & history effect RPI
If we risk factor-match the small (<50 mm) cases

Matched for diameter, gender and AAA history

<table>
<thead>
<tr>
<th></th>
<th>Stable</th>
<th>Repaired/Ruptured</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases [n]</td>
<td>27</td>
<td>27</td>
<td>-</td>
</tr>
<tr>
<td>Rupture Potential Index</td>
<td>0.47 ± 0.43</td>
<td>0.47 ± 0.22</td>
<td>0.1664</td>
</tr>
<tr>
<td>Peak wall stress [MPa]</td>
<td>0.33 ± 0.19</td>
<td>0.35 ± 0.15</td>
<td>0.2193</td>
</tr>
<tr>
<td>Growth rate [mm/yr]</td>
<td>2.68 ± 2.22</td>
<td>4.94 ± 2.67</td>
<td>0.0012</td>
</tr>
</tbody>
</table>

NO

Cases that ruptured or needed repair had similar RPI at baseline
Summary of initial findings

- We show a significant difference in baseline biomechanical indices between stable cases and those that ruptured or needed repair
  - No difference when looking at ALL small AAAs (< 50 mm)
  - No difference in matched cases (n=27)
    - Yet the ruptured/repaired cases still expanded much quicker

- Data very recently reported by Dutch group (retrospective study)
  - Significant difference in biomechanical indices in ruptured (n=45) and symptomatic (n=11) cases, compared to stable cases (n=175)
  - No difference after diameter-matching (n=31)
  - No added value of biomechanical indices

- Biomechanical methods are different but findings are similar

Leemans et al. PLOS One; 22 Aug 2018
What’s next?

- Continue the stats work and determine if RPI adds clinical value
- Combine with USPIO data (inflammation)
- A lot more simulation data ready to analyse
  - Uniform AAA wall thickness
    - MRI is expensive and not routine in AAA
  - Standardised blood pressure
- Continue to explore model fidelity and alternative parameters (geometry)
Thanks to the team and funding agency...

Nik Bappoo
Paul Norman
Jordan D’Souza
Simon Duong
Thomas Edland

Luke Falconer
Michael Millett
Quentin Bore
Chloe Dacher
Grand Joldes
Arjun Balaji

Rachael Forsythe
David Newby
Olivia McBride
Marc Dweck
Jenny Robson

Peter Hoskins
Noel Conlisk
Scott Semple
Calum Gray
Tom MacGillivray

& thank you for listening!

E: barry.doyle@uwa.edu.au
W: vasclab.mech.uwa.edu.au
@vasclab_uwa