Biomechanical Modeling of AAA Growth and rupture – A Clinical Perspective

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Disclosure

Speaker name:

..................................................JOY ROY..................................................

I have the following potential conflicts of interest to report:

☐ Consulting
☐ Employment in industry
☐ Stockholder of a healthcare company
☐ Owner of a healthcare company
☐ Other(s)

☑ I do not have any potential conflict of interest
Ruptures occur in small AAA

- 5-10% of ruptures - STAR Cohort (Unpublished data), RESCAN
- 4 times higher risk in women – UK SAT
- Ruptures in women are not decreasing

(Zomorodi et al., J Epidemiol Comm Health, 2018)
Ruptures occur in patients with known AAA

Can we find a better Predictor than Diameter to Predict

Rupture

Growth and the Need for Intervention

Quality of Life – debated
Biomechanical Risk Assessment

Wall thickness
- Long term blood pressure
- Overlying ILT

Relative expansion
- Gender
- Age

Wall stress
- Geometry
- Short term blood pressure
- ILT
- Wall thickness

Wall strength
- Gender
- Family history of ruptured AAA
- Thickness of overlying ILT
- Relative expansion

Rupture risk: Wall stress / Wall strength
Finite Element Modeling in AAA Growth and Rupture Prediction

- Challenge - Better than diameter

- Software that can be used in the clinical setting
  - easily accessible
  - reproducible
  - fast

- Wall stress
  - Wall stress/wall strength = rupture index

PWS = peak wall stress
PWRI = peak wall rupture index (Rupture
Proof of Concept Studies

Prediction of Rupture

Prediction of Growth/Need for Intervention
Proof of Concept Studies

Finite Element Analysis Derived

Parameters

Peak Wall stress

Peak Wall Rupture Index
Meta-analysis of peak wall stress in ruptured, symptomatic and intact abdominal aortic aneurysms

S. Khosla, D. R. Morris, J. V. Moxon, P. J. Walker, T. C. Gasser and J. Golledge

BJS 2014 – 9 articles

<table>
<thead>
<tr>
<th>Reference</th>
<th>Symptomatic or ruptured AAAs</th>
<th>Intact AAAs</th>
<th>Weight (%)</th>
<th>SMD (IV)</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>PWS N/cm²</td>
<td>Total</td>
<td>PWS N/cm²</td>
<td>Total</td>
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<tr>
<td>Vande Geest et al.</td>
<td>49.9(12.1)</td>
<td>9</td>
<td>46.0(9.5)</td>
<td>5</td>
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<tr>
<td>Gasser et al.</td>
<td>49.9(11.3)</td>
<td>8</td>
<td>46.0(9.6)</td>
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<tr>
<td>Fillinger et al.</td>
<td>35.2(12.6)</td>
<td>20</td>
<td>27.6(11.7)</td>
<td>30</td>
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<tr>
<td>Fillinger et al.</td>
<td>47.7(20.6)</td>
<td>10</td>
<td>36.9(8.8)</td>
<td>30</td>
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<td>Heng et al.</td>
<td>58.0(18.8)</td>
<td>22</td>
<td>42.0(12.5)</td>
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<td>Maier et al.</td>
<td>111.0(51.0)</td>
<td>30</td>
<td>67.0(30.0)</td>
<td>40</td>
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<td>Venkatasubramaniam</td>
<td>47.7(12.5)</td>
<td>23</td>
<td>34.3(10.5)</td>
<td>30</td>
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<tr>
<td>Truijers et al.</td>
<td>102.0(38.0)</td>
<td>12</td>
<td>62.0(28.0)</td>
<td>15</td>
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<tr>
<td></td>
<td>51.7(7.6)</td>
<td>10</td>
<td>39.7(10.4)</td>
<td>10</td>
</tr>
<tr>
<td>Total</td>
<td>144</td>
<td></td>
<td>204</td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: $I^2 = 0.00, \chi^2 = 5.23, 8$ d.f., $P = 0.73, I^2 = 0\%$

Test for overall effect: $Z = 8.05, P < 0.001$
Biomechanical Imaging Markers as Predictors of Abdominal Aortic Aneurysm Growth or Rupture: A Systematic Review


EJVES 2016

• 13 articles included Peak wall Stress.

• 10/13 articles PWS higher in rAAA compared to intact AAA

Conclusion

"Although PWS is significantly higher in symptomatic or ruptured AAAs in most FEA studies, confounding bias, clinical heterogeneity, and lack of standardisation limit the interpretation and generalisability of the results"
Prediction of Rupture

Stable

Pre-Rupture
Peak wall stress
101 patients – 14 months follow up
Rupture need for surgery

Limitations
Time consuming Finite Element Analysis
Thrombus - disregarded
Prediction of Rupture Sites in Abdominal Aortic Aneurysms After Finite Element Analysis

Philipp Erhart, MD¹, Joy Roy, MD², Jean-Paul P. M. de Vries, MD, PhD³, Moritz Lindquist Liljeqvist², Caspar Grond-Ginsbach, PhD⁴, Alexander Hyhlik-Dürr, MD, PhD¹, and Dittmar Böckler, MD, PhD¹

13 patients with rAAA.
- retrospective, multicentre
- pre rupture CT – within 2 years
- Heidelberg, Karolinska, Niewugein
Hypothesis
PWRR site corresponds to rupture site
PWRR is increased in pre-rupture CTs

7 of 13 patients- PWRR site corresponded to rupture site
Proof of concept paper – PWRR higher in pre-rupture AAA Vs Stable AAA

Retrospective but longitudinal
Only 13 patients

Erhart et al, JEVT 2016
Prediction of Growth and Need for Intervention

Growth

Need for Intervention
Volume vs Diameter Growth

41 patients

Diam: 39.1-64.4mm

Vol: 62.3-244.0 cm³

Baseline
- Maximal diameter
- Volume
- Peak wall stress = PWS
- Peak wall stress/wall strength ratio = PWRR

Follow-up
- Annual diameter growth rate [mm/year]
- Annual volume growth rate [cm³/year]

Volume and PWRI are better Predictors of Growth

**A**

- **AAA diameter growth rate [mm/year]**
- **AAA diameter growth rate [%/year]**

\[ r = 0.15, p = 0.34 \]
\[ r = -0.13, p = 0.41 \]

**B**

- **AAA volume growth rate [cm³/year]**
- **AAA volume growth rate [%/year]**

\[ r = 0.56, p = 0.0001 \]
\[ r = 0.36, p = 0.021 \]

**C**

- **PWRI Change [%/year]**

\[ r = 0.044 (-0.44 - 0.51), p = 0.86 \]

**D**

- **PWRI Change [%/year]**

\[ r = 0.70 (0.40 - 0.87), p = 0.0002 \]

- **Volume growth rate [cm³/year]**

\[ n = 18 \]
\[ n = 23 \]
Clinical diameter 40-50 mm
Baseline
95 patients (Ongoing) 4 yr FU after CT

- Clinical Maximal Diameter
- Semi-automatic 3D-segmentation och FEA
  - Diameters
  - Volumes
  - Biomechanical rupture risk PWRI

Growth Rate

n = 55:
Operation Indication
Surgery or
Diam ≥ 55 mm
diameter

n = 40:
”Stable”
No Surgery
Diameter < 55 mm
Semi Automatic Diameter and PWRI predict Growth

**PWRI**
- $r = 0.27, p = 0.0096$

**Clinical Diameter**
- $r = 0.17, p = 0.1$

**Semi-Aut Diam**
- $r = 0.41, p = 4.2e-05$
Need for Intervention

Liljevist Lindquist et al, Unpublished data
Prediction - Need for Intervention

Sensitivity

Clinical Diameter

3D/Biomechanical analysis:
- Ridge regression
- LASSO
- Logistisk regression

AUC

0.83 vs 0.73

P=0.023
The MA 3 RS Study Investigators
Circulation. 2017;136:787-797
The MA 3 RS Study: 50 patients

Conlisk et al. J Cardiovasc Transl Research 2017
Are All Software Equal? = Model Complexity

• In house software

• BioPARR
  Doyle et al, Scientific Reports 2017

• A4 Clinics, VASCOPS
  1 week to train a student with 10 sample AAAs
  10 students at our Center
  4 Regular users (Medical Doctors)
Take Home Messages

• 3 Dimensional Imaging should be performed during surveillance
  – CT
  – MRI – potential, contraindications, expense
  – 3 D Ultrasound – very interesting
  – PET – CT (F18 Sodium Fluoride)

- FEM and Semi Automatic Measurements – predict AAA growth and rupture better than Diameter
Present and Future Perspectives

• Prospective long term studies
  – 400 patients (200 male + 200 female) with 2 Cts during follow up

• Multicenter

• Improve AAA outcome prediction
  – Flow dynamics
  – Wall dynamics – strain
  – Fluid structure interaction – flow mechanics and wall mechanics

• Artificial Intelligence – Deep learning – speed up the process
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ki.se/mmk/star
ILT = good or bad?

Most AAAs contain an intraluminal thrombus (ILT), which may play dual roles:

- Cushions the vessel wall against mechanical stress
- Causes ECM degradation, hypoxia and vSMC apoptosis in the underlying wall

Can ILT morphology and quality affect its role?

Polzer et al, 2011, Eur J Vasc Endovasc Surg  
Talvitie et al, 2017
U – shaped relation between ILT thickness and AAA growth

Aneurysms without thrombus are more dependent on wall stress
PWRI and Semi-Automatic Diameters than to Clinical Diameter

Clinical Diameter

Semiautomatic External Diameter

PWRI

Diameter [mm]

Diameter [mm]

PWRI [ratio]

Annual Growth Rate [mm/year]

Annual Growth Rate [mm/year]

Annual Growth Rate [mm/year]

r = 0.17, p = 0.1

r = 0.41, p = 4.2e-05

r = 0.27, p = 0.0096

Liljevist Lindquist et al, Unpublished
Intraluminal Thrombus – effects on Growth

• 90 AAA patients with at least 2 CT measurements (6-24 months)
  – Karolinska University Hospital
  – Perugia, Italy

• A4 Clinics, VASCOPS – to measure local diameters of aortic wall, thrombus thickness and
Are All Software Equal? = Model Complexity

In house software

BioPARR
  – Doyle et al, Scientific Reports 2017

A4 Clinics, VASCOPS
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Take Home Messages

• 3 Dimensional Imaging
  – CT
  – MRI – potential, contraindications, expense
  – 3 D Ultrasound – very interesting
    ▪ FEM – predict AAA growth and rupture better than Diameter

▪ Clinical Gain
  ▪ Decrease cost of AAA surveillance
  ▪ Avoid Unnecessary AAA surgery in pts with high comorbidities
Present and Future Perspectives

• Prospective long term studies
  – 400 patients (200 male + 200 female) with 2 Cts during follow up

• Multicenter

• Improve AAA outcome prediction
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• Artificial Intelligence – Deep learning – speed up the process
Retrospektiv longitudinell studie

Klinisk diameter 40-50 mm vid baseline
Under surveillance vid vår klinik

95 patienter hittills

4 år uppföljning efter första DT

- Klinisk Maximal Diameter
- Semi-automatisk 3D-segmentering och FEA
  - Diametrar
  - Volymer
  - Biomekanisk rupturrisk, ‘PWRI’

Tillväxthastighet

Klinisk Diameter

n = 55:
Operationsindikation
Kirurgi eller ≥ 55 mm diameter

n = 40:
”Stabila”
Ingen kirurgi och < 55 mm diameter
Prediction of Need for Intervention

AUC

0.83 vs 0.73

P=0.023
PWRI and Semiautomatic
Diameters Superior to Clinical Diameter

Clinical Diameter [mm]
48
45
42

Stable
Surgery Indication

Prediction by PWRI and semiautomatic external diameter
- Predicted, 100 % spec
- Below thresholds

P = 0.023

Clinical Diameter
AUC = 0.75

Semiaut Diam + PWRI + ILT Thickness + An Vol AUC 0 = .86

Liljevist Lindquist et al, Unpublished