Biomechanical Indices for Rupture Risk Estimation in Abdominal Aortic Aneurysms

Eva L. Leemans, MSc1,2,3,4, Tineke P. Willems, MD, PhD5, Maarten J. van der Laan, MD, PhD1, Cornelis H. Slump, PhD4, and Clark J. Zeebregts, MD, PhD1

Abstract
Purpose: To review the use of biomechanical indices for the estimation of abdominal aortic aneurysm (AAA) rupture risk, emphasizing their potential use in a clinical setting. Methods: A search of the PubMed, Embase, Scopus, and Compendex databases was made up to June 2015 to identify articles involving biomechanical analysis of AAA rupture risk. Outcome variables [aneurysm diameter, peak wall stress (PWS), peak wall shear stress (PWSS), wall strain, peak wall rupture index (PWRI), and wall stiffness] were compared for asymptomatic intact AAAs vs symptomatic or ruptured AAAs. For quantitative analysis of the pooled data, a random effects model was used to calculate the standard mean differences (SMDs) with the 95% confidence interval (CI) for the biomechanical indices. Results: The initial database searches yielded 1894 independent articles of which 19 were included in the analysis. The PWS was significantly higher in the symptomatic/ruptured group, with a SMD of 1.11 (95% CI 0.93 to 1.26, p<0.001). Likewise, the PWRI was significantly higher in the ruptured or symptomatic group, with a SMD of 1.15 (95% CI 0.30 to 2.01, p=0.008). After adjustment for the aneurysm diameter, the PWS remained higher in the ruptured or symptomatic group, with a SMD of 0.85 (95% CI 0.46 to 1.23, p<0.001). Less is known of the wall shear stress and wall strain indices, as too few studies were available for analysis. Conclusion: Biomechanical indices are a promising tool in the assessment of AAA rupture risk as they incorporate several factors, including geometry, tissue properties, and patient-specific risk factors. However, clinical implementation of biomechanical AAA assessment remains a challenge owing to a lack of standardization.

Keywords
abdominal aortic aneurysm, biomechanical analysis, risk assessment, rupture, rupture risk index, symptomatic aneurysm, wall strain, wall stress

Introduction
Multiple risk factors contribute to the pathogenesis of abdominal aortic aneurysms (AAAs), including genetics, smoking habits, high blood pressure, diabetes mellitus, and hyperlipidemia.1 AAA rupture has a high mortality and morbidity, causing at least 10,000 deaths per year in the United States and 15,000 deaths per year in Europe.2 This risk of rupture can be minimized with elective repair, but both endovascular and surgical interventions carry the risk of mortality and morbidity.3 Consequently, there is a need of objective aneurysm rupture risk assessment that could reliably predict those AAAs with the highest risk and help select patients needing intervention. Diagnostic indices derived from medical imaging are used to create such an assessment. Currently, the maximum aneurysm diameter is used as a clinically relevant risk threshold for AAA rupture.1,4 In general, small (diameter <5.0 cm for women or <5.5 cm for men) and slowly expanding (<0.3 cm/y) aneurysms are less likely to rupture. Nonetheless, not every patient can be correctly categorized using the maximum

1Department of Surgery, Division of Vascular Surgery, University Medical Center Groningen, University of Groningen, the Netherlands
2Department of Biomechanical Engineering and Physics, Academic Medical Centre, Amsterdam, the Netherlands
3Department of Radiology, Academic Medical Centre, Amsterdam, the Netherlands
4MIRA Institute for Biomedical Engineering and Technical Medicine, University of Twente, Enschede, the Netherlands
5Department of Radiology, University Medical Center Groningen, University of Groningen, the Netherlands

Corresponding Author:
Clark J. Zeebregts, Department of Surgery, Division of Vascular Surgery, University Medical Center Groningen, University of Groningen, PO Box 30 001, 9700 RB Groningen, the Netherlands.
Email: czeebregts@hotmail.com
AAA diameter, as illustrated by the fact that each year 2% of the small aneurysms rupture, while ~80% of large aneurysms remain stable. Therefore, additional patient-specific diagnostic indices must be found to better estimate potential aneurysm rupture.

Biomechanical analyses can provide new indices that incorporate both morphological and hemodynamic variables. These analyses are based on a basic principle of material failure: an aneurysm ruptures when wall stresses exceed wall strength. In vessels, 2 types of stress (force per unit area) occur. First, the blood pressure produces an in-plane wall stress resulting in wall deformation. Second, the movement of the blood along the vessel causes a shear stress parallel to the wall. As the vessel wall changes the elasticity changes. The wall strength can be estimated using strain or wall displacement measurements that can be derived from real time dynamic imaging, such as ultrasound or cardiac-gated computed tomography (CT).

Subsequently, a rupture index can be calculated by dividing calculated wall stress by the estimated wall strength. Using computational models, new indices can be extracted from diagnostic imaging, such as CT or magnetic resonance imaging (MRI). In this manner, several new patient-specific indices have become available, such as peak wall stress (PWS), peak wall shear stress (PWSS), wall strain, and the peak wall rupture index (PWRI). However, the clinical applicability and the additional value of these indices compared with the maximum diameter are still unknown. To shed light on these areas, a review was conducted of the current literature on biomechanical analysis for the estimation of AAA rupture risk. A meta-analysis was performed to compare the biomechanical indices between patients with asymptomatic intact AAA and those with symptomatic or ruptured AAAs.

**Methods**

**Literature Search**

One author (E.L.L.) performed the initial literature search to identify articles involving biomechanical analysis of AAA rupture risk. Based on a predefined search strategy devised according to the 2009 Preferred Reporting Items for Systematic reviews and Meta-Analysis (PRISMA) statement, the PubMed, Embase, Scopus, and Compendex databases were queried from inception to June 2015 using the following search terms: “abdominal aortic aneurysm,” “biomechanical analysis,” “peak wall stress,” “peak wall shear stress,” and “strain.” There were no limitations with regards to language, publication status, article type, or publication year.

The titles and abstracts from the initial search results were reviewed. Articles were excluded based on the following criteria: (1) AAA not the focus of the study, (2) no relation to rupture risk, (3) only in vitro or non–patient-specific methods used, (4) no diagnostic imaging or biomechanical indices employed, (5) thoracic or repaired aneurysms involved, (6) no English or Dutch translation available, and (7) no full text available. Discrepancies among the authors during full text review were resolved by discussion and consensus. Case reports, letters, reviews, commentaries, and duplicate items were eliminated. Reference lists of initially selected articles were screened to increase the yield of relevant publications.

**Quality Assessment**

Methodologic quality of the included studies was assessed using the Newcastle-Ottawa score (NOS). Quality was scored in 3 categories: selection, comparability, and exposure or outcome. Per category a study was assigned a maximum of 4, 2, and 3 points, respectively. Studies of good quality scored the maximum of 2 points for the comparability category and >2 points for the other categories or >6 points in total. Studies of poor quality scored 0 or 1 point per category or <4 points in total. Publication bias was assessed with a funnel plot of the logarithmic effect size vs the standard error for each biomechanical index.

**Data Extraction**

The following study and computational variables were recorded: article type, aim of the study, imaging method, biomechanical analysis method, analysis software(s), inclusion of calcification and intraluminal thrombus (ILT) into the computational model, and the biomedical indices (PWS, PWSS, PWRI, wall stiffness, wall strain). Furthermore, the following demographic variables were recorded: population size (asymptomatic intact AAA, symptomatic AAA, and ruptured AAA); smoking status; gender; blood pressure; and the maximum AAA diameter.

**Statistical Analysis**

The outcomes of asymptomatic intact AAAs vs symptomatic or ruptured AAAs were compared. Data were reported as the mean ± standard deviation. If a study represented the data as ± standard error, it was converted to standard deviation for uniform data interpretation. For each included study, a separate comparison was done using a 2-sample t test; p<0.05 was considered the threshold of statistical significance.

Standard mean differences (SMDs) were calculated with the 95% confidence interval (CI) for each study using inverse variance random effect models to reduce the effect of heterogeneity in biomechanical analysis methods on the summary statistics. The interstudy heterogeneity was assessed by means of the I² index, which describes the percentage of
variability in effect estimates due to heterogeneity. $I^2$ values >75% indicated considerable heterogeneity. A subanalysis evaluated the results in the diameter-controlled groups. Statistical analysis was performed using Review Manager 5.3 (Cochrane Information Management System; http://ims.cochrane.org/revman).

**Results**

**Study Selection and Characteristics**

The initial database searches yielded 1894 studies (Figure 1), from which 1549 studies were culled based on title and abstract. The main reasons for exclusion at this level were lack of purely infrarenal AAA subjects or inclusion of AAA patients after treatment. During full text screening, 326 articles were excluded mainly because they did not compare asymptomatic intact AAAs with ruptured/symptomatic AAAs.

The 19 included studies employed 2 types of computational strategies to calculate wall stress; 14 studies used finite element analysis (FEA) to measure PSW and 3 studies used fluid-structure interaction (FSI) to measure PWSS. FEA is a numerical method to find the approximate solution of a complex biomechanical problem, such as calculating the stress (mechanical loading) on AAA geometry. Several software packages are available to compute FEA, and an example is displayed in Figure 2. FSI uses several computational strategies to determine the interaction of a fluid with the surroundings, ie, the blood flow with the arterial wall. Only 2 studies assessed wall strength by evaluating strain using ultrasound.

Study characteristics and quality scores are displayed in Table 1. Six studies scored low in one or more categories of the NOS quality assessment. Only 3 studies had a high NOS score in each category. However, all included studies were of fair to good quality according to the total NOS scores. The funnel plots to assess publication bias could not be appraised accurately due to the small number of studies.

Baseline characteristics of the included studies showed similar patient age in all groups (range 49–96 years old). All studies examined populations from the United States and Europe. More males than females were included but often the fraction of females in the ruptured group was higher compared with the asymptomatic intact group. The percentage of smokers was reported in only 6 studies, but it was equally distributed between groups.

---

**Figure 1.** PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analysis) flow diagram.
All FEA and FSI studies used CT to acquire the AAA geometry; both wall strength studies used ultrasound. The biomechanical index was measured before the onset of rupture in 6 articles and after in 7 studies; for 6 studies, the acquisition moment was unclear. Five FEA studies reported the PWS and PWSS, respectively, in groups matched by maximum diameter. Sample size in these studies ranged from 3 to 282 in the intact (AAA), 1 to 40 in the ruptured, and 0 to 15 in the symptomatic groups.

**Meta-analysis**

The PWS was reported in N/cm², which required conversion from MPa or kPa in 5 studies. Two of the included studies reported an insignificant difference in PWS between the ruptured group and the intact AAA group (p=0.524 and p=0.535). The combined analysis of 14 studies contained 247 ruptured/symptomatic AAAs and 503 asymptomatic intact AAAs. The PWS was significantly higher in the symptomatic/ruptured group, with a SMD of 1.11.

**Table 1. Overview of Selected Studies Grouped by Computational Strategy or Biomedical Index.**

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Software</th>
<th>ILT</th>
<th>Ca</th>
<th>AAA</th>
<th>RAAA</th>
<th>SAAA</th>
<th>S</th>
<th>C</th>
<th>O</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Finite element analysis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fillinger, 2002¹²</td>
<td>ABAQUS</td>
<td>N</td>
<td>N</td>
<td>48</td>
<td>10</td>
<td>8</td>
<td>3</td>
<td>2</td>
<td>3</td>
<td>8</td>
</tr>
<tr>
<td>Fillinger, 2003¹³</td>
<td>ABAQUS</td>
<td>N</td>
<td>N</td>
<td>42</td>
<td>14</td>
<td>8</td>
<td>3</td>
<td>1</td>
<td>3</td>
<td>7</td>
</tr>
<tr>
<td>Venkatasubramaniam, 2004¹⁴</td>
<td>ANSYS</td>
<td>N</td>
<td>N</td>
<td>15</td>
<td>12</td>
<td>—</td>
<td>2</td>
<td>2</td>
<td>3</td>
<td>7</td>
</tr>
<tr>
<td>Raghavan, 2005¹⁵</td>
<td>ANSYS</td>
<td>N</td>
<td>N</td>
<td>14</td>
<td>17</td>
<td>—</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>Vande Geest, 2006¹⁶</td>
<td>ABAQUS</td>
<td>N</td>
<td>N</td>
<td>5</td>
<td>8</td>
<td>—</td>
<td>3</td>
<td>0</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>Truijers, 2006¹³</td>
<td>ABAQUS</td>
<td>N</td>
<td>N</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>3</td>
<td>1</td>
<td>3</td>
<td>7</td>
</tr>
<tr>
<td>Vande Geest, 2008¹⁸</td>
<td>ABAQUS</td>
<td>N</td>
<td>N</td>
<td>5</td>
<td>9</td>
<td>—</td>
<td>3</td>
<td>0</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>Heng, 2008¹⁹</td>
<td>ANSYS</td>
<td>N</td>
<td>N</td>
<td>40</td>
<td>30</td>
<td>—</td>
<td>3</td>
<td>1</td>
<td>3</td>
<td>7</td>
</tr>
<tr>
<td>Gasser, 2010²³</td>
<td>VASCOPS</td>
<td>Y</td>
<td>N</td>
<td>30</td>
<td>20</td>
<td>—</td>
<td>3</td>
<td>2</td>
<td>3</td>
<td>8</td>
</tr>
<tr>
<td>Doyle, 2010²¹</td>
<td>ABAQUS</td>
<td>Y</td>
<td>N</td>
<td>42</td>
<td>17</td>
<td>—</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>Reeps, 2010²⁰</td>
<td>HARPOON</td>
<td>Y</td>
<td>Y</td>
<td>3</td>
<td>1</td>
<td>—</td>
<td>2</td>
<td>0</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Maier, 2010²²</td>
<td>HARPOON</td>
<td>Y</td>
<td>N</td>
<td>30</td>
<td>14</td>
<td>9</td>
<td>3</td>
<td>1</td>
<td>3</td>
<td>7</td>
</tr>
<tr>
<td>Gasser, 2014²⁴</td>
<td>VASCOPS</td>
<td>Y</td>
<td>N</td>
<td>203</td>
<td>40</td>
<td>—</td>
<td>3</td>
<td>1</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>Erhart, 2015²⁵</td>
<td>VASCOPS</td>
<td>Y</td>
<td>N</td>
<td>30</td>
<td>15</td>
<td>15</td>
<td>3</td>
<td>0</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>Fluid-structure interaction</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Xenos, 2010²⁶</td>
<td>Adina</td>
<td>Y</td>
<td>Y</td>
<td>8</td>
<td>2</td>
<td>—</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Xenos, 2010²⁶</td>
<td>Adina</td>
<td>Y</td>
<td>Y</td>
<td>8</td>
<td>2</td>
<td>—</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Xenos, 2014²⁸</td>
<td>Adina</td>
<td>Y</td>
<td>Y</td>
<td>8</td>
<td>2</td>
<td>—</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>Wall strain</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sonesson, 1999²⁹</td>
<td>Diamove US tracking</td>
<td>121</td>
<td>11</td>
<td>—</td>
<td>3</td>
<td>0</td>
<td>1</td>
<td>4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wilson, 2003²⁸</td>
<td>Diamove US tracking</td>
<td>282</td>
<td>28</td>
<td>—</td>
<td>4</td>
<td>2</td>
<td>2</td>
<td>8</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: AAA, abdominal aortic aneurysm; Ca, calcium; ILT, intraluminal thrombus; N, no; Y, yes; NOS, Newcastle-Ottawa Score; S, selection (maximum 4); C, comparability (maximum 2); O, outcome/exposure (maximum 3); RAAA, ruptured AAA; SAAA, symptomatic AAA; US, ultrasound.

**Figure 2.** Geometry reconstruction and mesh generation by A4research (VASCOPS). (A) Initialization by manually selecting the iliac arteries and evolution of the active shape, (B) lumen segmentation, and (C) external segmentation. The blocks represent the mesh elements.
Furthermore, a low heterogeneity between studies was seen ($I^2=9\%$). Five studies$^{12,15,21-23}$ controlled for possible effects of the diameter by eliminating the smallest (maximum diameter <50–55 mm) and the largest (maximum diameter >75–80 mm) AAA, thus not only minimizing the effect of diameter on the biomechanical indices but also eliminating the cases for which the need to treat was already clear. Four$^{12,15,21,22}$ of these studies were included in the subanalysis as one study$^{23}$ did not report quantitative data for the cases matched by maximum AAA diameter. In total, 55 patients in the ruptured/symptomatic group and 61 patients in the asymptomatic AAA group were included in the subanalysis. Three studies$^{25,26,28}$ showed significant differences between groups. Combined analysis of the diameter-controlled studies also showed a significantly higher PWS in the ruptured/symptomatic group, with a SMD of 0.85 (95% CI 0.46 to 1.23, p<0.001; Figure 3B) and a low heterogeneity ($I^2=0\%$). However, considerable heterogeneity between the studies was seen ($I^2=89\%$). Only one$^{23}$ of the studies examining PWRI corrected for diameter, but no quantitative data were reported.

Eight studies determined a rupture index employing 3 methods: FEA rupture index,$^{21}$ peak wall rupture index (PWRI)$^{23,25,27}$ and the rupture potential index (RPI)$^{16,25,26,28}$ Three studies$^{26-28}$ used FSI instead of FEA to calculate the rupture index, but no quantitative data were reported. Analysis of the studies assessing PWRI with FEA contained 90 ruptured/symptomatic cases and 263 asymptomatic AAAs. Only one$^{23}$ of the studies showed no significant differences between groups (p=0.06). The combined analysis (Figure 3C) showed a significantly higher PWRI in the ruptured/symptomatic group, with a SMD of 1.15 (95% CI 0.30 to 2.01, p=0.008). However, considerable heterogeneity between the studies was seen ($I^2=89\%$). Only one$^{23}$ of the studies examining PWRI corrected for diameter, but no quantitative data were reported.

Three studies$^{25,26,28}$ reported the PWSS for AAAs vs ruptured/symptomatic AAAs. The results showed a trend toward a higher PWSS in ruptured aneurysms. However, the studies included only a few patients and only 1 study$^{28}$ reported quantitative data, so a combined analysis could not be done.

Only 2 studies$^{8,29}$ compared the wall stiffness between ruptured/symptomatic aneurysms and AAAs, despite the fact that the possibilities of wall stiffness measurements

---

**Figure 3.** Forest plots for (A) the peak wall stress (N/cm²), (B) diameter-matched peak wall stress (N/cm²), and (C) the peak wall rupture index. AAA, abdominal aortic aneurysm; CI, confidence interval; IV, inverse variance; rAAA, ruptured AAA.
are increasing. The results showed no significant difference in wall stiffness between the asymptomatic and ruptured groups. However, a decrease of stiffness over time was significantly correlated with rupture. Only median and range were reported, thus a pooled analysis was not performed.

**Discussion**

Over the past decades, biomechanical analysis for estimating AAA rupture risk has gained scientific popularity. This ongoing scientific work has resulted in a broad range of available biomechanical indices. However, the results of the analytical methods are influenced by the inputs (imaging and segmentation method, wall properties (tensile strength and inclusion of ILT and calcifications), and the boundary conditions (pressure configuration, AAA contact points, flow conditions). Therefore, careful and consistent selection is needed to get the most accurate and clinically valuable results. Standardization of the presented technologies starts with consistent reporting of these boundary conditions, for instance, using the methodology as stated by Erdemir et al.

FEA was the most popular method. However, the popularity and possibilities of flow and strain measurements are increasing as more sophisticated imaging methods become available, such as phase contrast MRI. These techniques not only provide real-time flow and wall movement data but could also be used to create patient-specific boundary conditions for the biomechanical computational models.

The analysis methods are improving, but the number of available biomechanical indices is also increasing. For instance, during a large retrospective trial, Gasser et al showed that PWS increases linearly and PWRI increases exponentially with diameter, which made possible the introduction of the rupture risk equivalent diameter (RRED). This value denotes the maximum aneurysm diameter of an average patient with the same PWRI (Figure 4). This new index facilitates incorporation of biomechanics in daily clinical practice, as the interpretation of RRED is similar to the maximum diameter measure.

However, only a limited number of studies compared asymptomatic intact with ruptured/symptomatic AAAs. Therefore, the quantitative analysis could assess only 2 biomechanical indices: PWS and PWRI. Both indices were significantly higher in ruptured cases compared to asymptomatic cases. The diameter-matched groups also showed a significant difference. However, a large overlap between groups was seen. These findings support the use of biomechanical analysis for rupture risk assessment; while aneurysm diameter is important, other factors play a role as well.

**Limitations**

These results must be viewed in the context of their limitations. First, the participant selection, imaging moment, and model conditions differed between studies and were not carefully reported in some cases. Furthermore, although the statistical model corrected for the heterogeneity between studies, a significant and large statistical heterogeneity between the PWRI studies was seen. Therefore, further analyses with standardized, accurate models are needed to truly facilitate the translation of this technology into daily clinical practice. Also, publication bias could be present as funnel plots could not be appraised due to the limited number of studies.

Most studies retrospectively included asymptomatic, symptomatic, and ruptured AAA cases. This has drawbacks as the asymptomatic intact AAA could have ruptured if no repair was done. Thus, without repair they might have ended up in the ruptured group, while with repair the ruptured cases could have ended in the intact group. A prospective trial with sufficient sample sizes is needed to truly assess the differences in biomechanical indices between groups. In addition, an interest exists in following aneurysm development and accompanying biomechanics over time, for instance during growth.

Another concern is the variability of the analysis. Recent studies showed that the observer variability of one FEA model was low, and a large observer agreement was present. However, most other models are not tested for observer variability, limiting the confidence of the index measured with these models.

Finally, the clinical applicability in addition to the maximum AAA diameter is still unknown. Fillinger et al showed that PWS was superior to diameter in predicting
rupture. However, a large overlap between groups was seen in that study and our own. Receiver operating characteristic curves for predicting rupture showed the best sensitivity, specificity, and accuracy (94%, 81%, and 85%, respectively) at a threshold of 44 N/cm². Such a threshold for repair simplifies the clinical implementation but needs further verification.

Conclusion
Biomechanical analysis is a promising tool in the assessment of AAA rupture risk as it incorporates several factors including geometry, tissue properties, and patient-specific risk factors. The lack of standardization though, limits the translation of this technique to clinical practice.

Acknowledgments
We would like to thank Ruben V. C. Buijs for his support and ideas during the research.

Declaration of Conflicting Interests
The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding
The author(s) received no financial support for the research, authorship, and/or publication of this article.

References