Finite Element Analysis in Asymptomatic, Symptomatic, and Ruptured Abdominal Aortic Aneurysms: In Search of New Rupture Risk Predictors

P. Erhart [a,*,e], A. Hyhlik-Dürr [a,e], P. Geisbüsch [a], D. Kotelis [a], M. Müller-Eschner [b], T.C. Gasser [c], H. von Tengg-Kobligk [b,d], D. Böckler [a]

[a] Department of Vascular and Endovascular Surgery, Ruprecht-Karls University Heidelberg, Germany
[b] Department of Radiology, Ruprecht-Karls University Heidelberg, Germany
[c] Department of Solid Mechanics, Royal Institute of Technology, Stockholm, Sweden
[d] Institute of Diagnostic, Interventional and Pediatric Radiology, University Hospital Bern, Inselspital, Bern, Switzerland

WHAT THIS PAPER ADDS

To evaluate finite element analysis (FEA) as a predictive risk model for abdominal aortic aneurysm (AAA) rupture, a single center retrospective analysis was performed to compare biomechanical properties in asymptomatic, symptomatic, and ruptured AAAs. Peak Wall Rupture Risk Index (PWRI) differentiates subgroups better than Peak Wall Stress (PWS). These preliminary results suggest that AAA patients with PWRI values greater than 1.0 may be at imminent risk of becoming symptomatic or even rupturing.

Objectives: To compare biomechanical rupture risk parameters of asymptomatic, symptomatic and ruptured abdominal aortic aneurysms (AAA) using finite element analysis (FEA).
Study design: Retrospective biomechanical single center analysis of asymptomatic, symptomatic, and ruptured AAAs. Comparison of biomechanical parameters from FEA.
Materials and methods: From 2011 to 2013 computed tomography angiography (CTA) data from 30 asymptomatic, 15 symptomatic, and 15 ruptured AAAs were collected consecutively. FEA was performed according to the successive steps of AAA vessel reconstruction, segmentation and finite element computation. Biomechanical parameters Peak Wall Rupture Risk Index (PWRI), Peak Wall Stress (PWS), and Rupture Risk Equivalent Diameter (RRED) were compared among the three subgroups.
Results: PWRI differentiated between asymptomatic and symptomatic AAAs ($p < .0004$) better than PWS ($p < .1453$). PWRI-dependent RRED was higher in the symptomatic subgroup compared with the asymptomatic subgroup ($p < .0004$). Maximum AAA external diameters were comparable between the two groups ($p < .1355$). Ruptured AAAs showed the highest values for external diameter, total intraluminal thrombus volume, PWS, RRED, and PWRI compared with asymptomatic and symptomatic AAAs. In contrast with symptomatic and ruptured AAAs, none of the asymptomatic patients had a PWRI value >1.0. This threshold value might identify patients at imminent risk of rupture.
Conclusions: From different FEA derived parameters, PWRI distinguishes most precisely between asymptomatic and symptomatic AAAs. If elevated, this value may represent a negative prognostic factor for asymptomatic AAAs.

Keywords: Aorta, Finite element analysis (FEA), Rupture risk, Abdominal aortic aneurysm, Wall stress

INTRODUCTION

Precise prediction of rupture in patients with abdominal aortic aneurysms (AAA) continues to be a problem. In routine clinical practice the maximum aortic diameter is the criterion most often used for AAA repair. The ESVS guideline (European Society of Vascular Surgery) reports an exponentially increasing annual rupture risk for patients exceeding diameters of 5.0—5.5 cm.[1] However, this sole parameter does not necessarily reflect the true risk of rupture in each patient.

The potential for several additional parameters, including the geometrical AAA shape,[2] female gender,[3,4] arterial hypertension,[5] smoking history,[6] familial AAA predisposition,[7] and large amount of intraluminal thrombus formation,[8] to elevate the individual rupture risk has been discussed, but these are rarely included in clinical decision making regarding AAA repair. The finite element analysis (FEA) software used in this study incorporates patient specific risk factors to calculate biomechanical rupture risk indices with

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[e] The first two authors contributed equally to the article.
* Corresponding author. P. Erhart, Department of Vascular and Endovascular Surgery, Ruprecht-Karls University Heidelberg, Im Neuenheimer Feld 110, 69120 Heidelberg, Germany.

a high investigator reproducibility,[9,10] thus having the potential to predict patient specific AAA rupture risk more precisely than maximum aortic diameter alone.[11] Clinical and experimental studies are still required to examine accuracy of the described FEA model.

The aim of this study was to compare biomechanical parameters from FEA in patients with asymptomatic, symptomatic, and ruptured AAAs to evaluate the predictive value of FEA in AAA rupture risk assessment.

METHODS

Study population

Computed tomography angiography (CTA) data from 60 patients with asymptomatic ($n = 30$ [all men], age 71 [50—86]), symptomatic ($n = 15$ [11 men], age 75 [49—85]), and ruptured AAAs ($n = 15$ [14 men], age 73 [60—88]) treated at a single center between 2011 and 2013 were selected consecutively according to the date of CTA investigation, and analyzed retrospectively. Vessel wall angulation is a limiting factor that disturbs FEA generation in asymptomatic and symptomatic AAAs. In addition, contrast extravasation complicates FEA generation in ruptured AAAs. If FEA generation was impossible in a certain case, this patient was excluded from the study and CTA data for the next patient was analyzed, until the predefined study population size was reached.

Patient characteristics are shown in Table 1. Inclusion criteria were elective repair of AAA with maximum diameter >5.0 cm without symptoms or signs of rupture on the preoperative CTA in the asymptomatic AAA group, and extravasation of contrast medium and/or retroperitoneal hematoma on CTA for the ruptured AAA group. Patients with AAA associated symptoms, for example abdominal and/or back pain who were undergoing prompt AAA repair after ruling out other differential diagnoses and who did not have CTA morphological signs of rupture, were assigned to the symptomatic AAA group. FEA was generated and compared from CTAs of non-ruptured (asymptomatic and symptomatic AAA group) and ruptured CTAs (ruptured AAA group). All patients underwent either open surgical or EVAR repair.

CTA scans of the abdominal aorta were acquired with a 64 slice CT scanner using standard radiologic parameters (in plane resolution 0.33 mm, slice thickness 0.7—1.0 mm). Both elective and emergency CTA for asymptomatic, symptomatic and ruptured AAAs were generated within this protocol. Brachial systolic blood pressure (Riva-Rocci) was recorded in all patients with ruptured AAAs during emergency CTA diagnostics. For asymptomatic and symptomatic AAAs, a systemic blood pressure of 130/80 mmHg was assumed. Patient specific risk factors like gender, smoking history, and arterial hypertension were collected in all groups for retrospective FEA. This study was permitted by the local ethics committee.

Finite element model

FEA was performed by a single experienced investigator using the DICOM data format of CTA. Commercially available CE certified semi-automatic analyzing software (A4clinics; VASCOPS GmbH, Graz, Austria) was used. Analysis was based on the three subsequent steps of AAA vessel wall reconstruction from CTA data, segmentation (i.e. mesh generation) and calculation of morphological (diameter/volume measurements) and biomechanical parameters (PWS, PWRI, RRED). Reconstruction of AAA morphology was semi-automatic, allowing capture of external and contrasted internal vessel surfaces. Both the external vessel wall and intraluminal thrombus (ILT) were divided into voxels for subsequent biomechanical calculation. In all patients FEA was performed between the renal arteries and the aortic bifurcation.[11] The effects of ILT and AAA wall properties were described by previously suggested isotropic models.[11] Specifically, all FEA model properties (wall thickness, mesh size, constitutive tissue properties, etc.) were homogenous in all AAA subgroups, and details regarding image segmentation have been reported before.[12] The following mechanical and geometrical parameters were calculated:

- Peak Wall Stress (PWS): Tensile stress exerted on the vessel wall based on aneurysm shape, diameter and blood pressure values. The maximal value (in kilo Pascal) within an AAA corresponds to the PWS.
- Peak Wall Rupture Index (PWRI): This index relates tensile stress (PWS) to vessel wall strength (PWRI = PWS/wall strength) and additionally incorporates patient specific risk factors like gender and intraluminal thrombus. The PWRI value ranges from 0.0

Table 1. Patient characteristics and co-morbidities of AAA subgroups.

	Asymptomatic AAAs ($n = 30$)	Symptomatic AAAs ($n = 15$)	Ruptured AAAs ($n = 15$)
Age	71 (50—86)	75 (49—85)	73 (60—88)
Male sex	30 (100%)	11 (73%)	14 (93%)
Arterial hypertension	29 (97%)	13 (87%)	12 (80%)
Smoking history	20 (67%)	5 (33%)	8 (53%)
Coronary heart disease	12 (40%)	8 (53%)	6 (40%)
Dyslipidemia	10 (33%)	4 (27%)	1 (7%)
Peripheral arterial occlusive disease	4 (13%)	1 (7%)	2 (13%)
BP systolic during CTA (in mmHg)	130 assumed	130 assumed	126 (80—170)
BP diastolic during CTA (in mmHg)	130 assumed	130 assumed	74 (50—80)

Absolute and median values ± standard deviation, (lowest—highest values) are shown.CTA = computer tomography angiography; BP = blood pressure.

to infinity. In theory, a PWRI of 1.0 means rupture in an average specimen.
- Rupture Risk Equivalent Diameter (RRED): Correlation of the PWRI to the "average AAA population" (millimeters).
- Maximum AAA diameter (millimeters).
- Intraluminal Thrombus Volume (ILT volume) (centimeters^3).

The PWRI refers to the greatest wall rupture risk index, which is converted into the RRED automatically. The RRED was introduced to quantify the individual rupture risk. It corresponds to a fictitious diameter of an "average AAA" with the same risk of rupture (i.e. the same PWRI).[13] Thus the RRED links the individual biomechanical rupture risk profile to clinical AAA diameter based studies.

Vessel morphology reconstruction is impaired in patients with complex AAA morphology (angulation) or massive contrast extravasation in case of rupture.

Data analysis

Statistical analysis was performed with GraphPad Prism Version 4 (GraphPad Software, Inc.; La Jolla, CA, USA).

Mean ± standard deviations were calculated for each subgroup. A Kruskal-Wallis test illustrated differences between the three subgroups (see Fig. 1). To compare asymptomatic and symptomatic AAA subgroups, the Mann-Whitney test was used.

RESULTS

FEA generation was performed in 30 asymptomatic, 15 symptomatic, and 15 ruptured AAAs. Because of complex vessel morphology or contrast extravasation, two asymptomatic, three symptomatic, and nine ruptured AAAs were excluded and consecutively performed CTA were used for FEA until study population size was

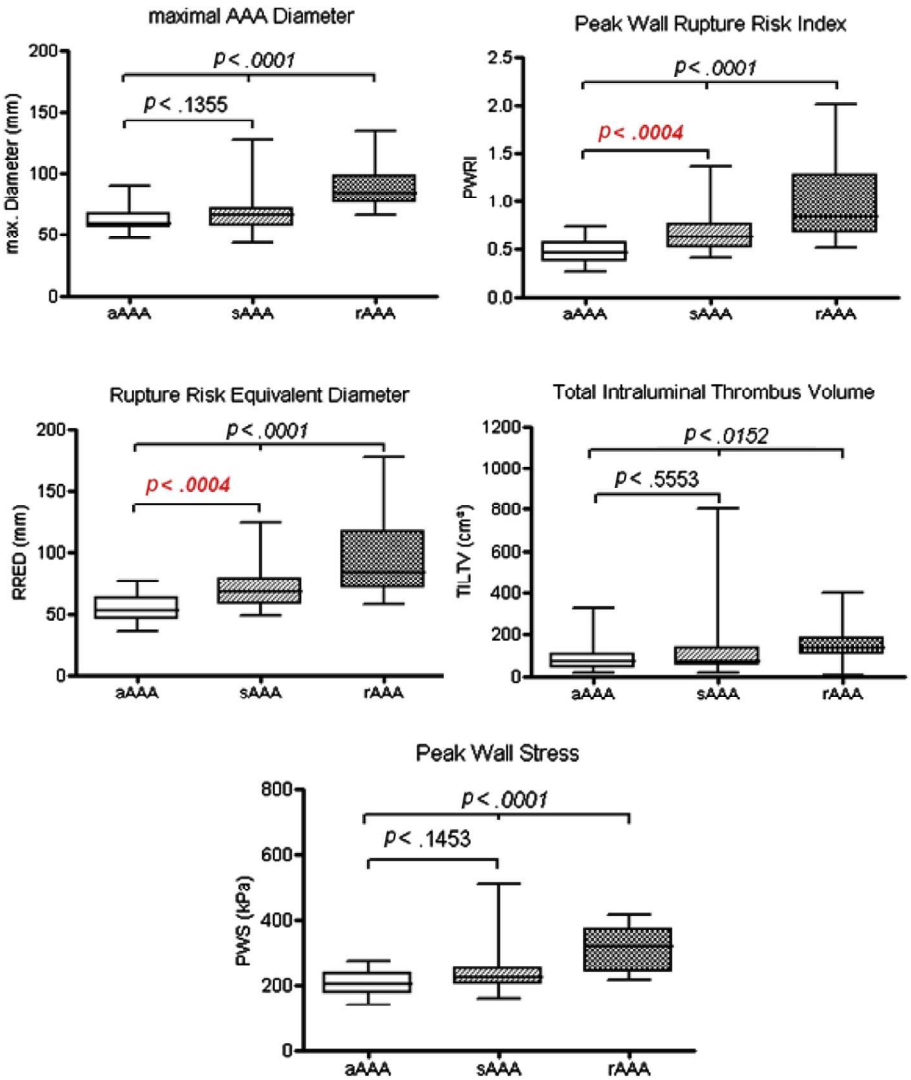

Figure 1. Parameters of asymptomatic, symptomatic, and ruptured AAAs from FEA. Maximum AAA diameter, Total Intraluminal Thrombus Volume (TILTV), Peak Wall Stress (PWS), Rupture Risk Equivalent Diameter (RRED), and Peak Wall Rupture Risk (PWRI) are shown. In ascending order these parameters were significantly increased and highest in ruptured AAAs (Kruskal-Wallis analysis compares all subgroups). Asymptomatic AAAs and symptomatic AAAs showed comparable external AAA diameters. Retrospective analysis of asymptomatic and symptomatic AAA patients revealed significant differences in PWRI and RRED (red *p* values; Mann-Whitney test). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

reached. In all patients FEA could be performed within 15–30 minutes.

In ascending order asymptomatic, symptomatic, and ruptured AAAs revealed higher PWS ($p < .0001$), PWRI ($p < .0001$), amount of intraluminal thrombus ($p < .0152$), external AAA diameter ($p < .0001$), and RRED ($p < .0001$) (see Table 2 and Fig. 1). Thus patients with symptomatic or ruptured AAAs showed an increased biomechanical rupture risk profile compared with asymptomatic patients. None of the asymptomatic AAA group showed PWRI values >1.0, in contrast with one symptomatic and four ruptured AAAs. PWRI values >0.5 were found in 40% of asymptomatic, 87% of symptomatic, and all ruptured AAAs.

Symptomatic AAAs showed significantly increased PWRI values ($p < .004$) and PWRI based RRED ($p < .004$) compared with asymptomatic patients. Although maximal AAA external diameters were comparable within these two subgroups ($p < .1355$), RREDs were higher in patients with symptomatic AAAs (see Fig. 2).

In seven patients from the ruptured AAA group contrast extravasation was visible on the CTA, whereas retroperitoneal hematoma was present on the remaining eight CTAs. If present, FEA detected rupture sites, defined as sites of contrast extravasation consistently. As rupture sites are devoid of an intact vessel wall, local rupture risk from FEA was zero (see Fig. 3). The software analyzed each segmented AAA voxel independently, so that a distant rupture site did not affect FEA computation of adjacent intact AAA wall regions.

DISCUSSION

This study showed that retrospective FEA revealed biomechanical differences in asymptomatic, symptomatic and ruptured AAAs. PWRI and RRED appear to be the most sensitive parameters to differentiate asymptomatic and symptomatic AAAs. A PWRI >1.0 means rupture of an "average AAA specimen" in theory.[10,11] Although not every symptomatic or ruptured AAA in the present study exceeded this value, PWRI may identify AAA patients with high rupture risk potential. Until now no biomechanical threshold value has been introduced for rupture risk assessment. To detect asymptomatic patients at risk, a critical PWRI value <1.0 should be proposed for further validation. According to the present observations, a PWRI of 0.5 may be appropriate for further verification, as all patients with ruptured and 87% of symptomatic AAAs had PWRI values >0.5.

PWS and PWRI in ascending order were significantly elevated in symptomatic and ruptured AAAs compared with the asymptomatic patients. The resulting RRED was highest in the ruptured AAA group. AAAs exceeding 5.5 cm in diameter are concordantly accepted for elective surgical repair in males; however, use of this as the sole parameter is highly controversial,[14] as several studies have shown that rupture occurs in AAA diameters <5.5 cm[15] and may never occur in other AAAs exceeding 5.5 cm.[16] Depending on the individual biomechanical properties, external AAA diameters may be different from their corresponding rupture risk equivalent diameters (RRED). The amount of intraluminal thrombus was significantly increased in symptomatic and ruptured AAAs. A large intraluminal thrombus volume is believed to disrupt the local AAA wall integrity;[17] however, its effect on wall stress is undetermined.[18–22]

A tendency for higher Peak Wall Stress (PWS) and Peak Wall Rupture Risk Index (PWRI) had already been identified in ruptured AAAs compared with non-ruptured AAAs,[11,23] whereas PWRI discriminated slightly better between the two subgroups.[11] In this study, the greatest AAA diameters were found in the ruptured AAA group, implicating a great influence of the external AAA diameter on FEA calculation. Both PWS and PWRI values are diameter dependent. Therefore comparison of the biomechanical parameters between ruptured and non-ruptured AAAs may be inaccurate in this study. As external AAA diameters were comparable between asymptomatic and symptomatic patients, comparison of the non-ruptured subgroups may be more relevant. PWRI and RRED from FEA turned out to be the most critical parameters to distinguish between patients with asymptomatic and symptomatic AAAs ($p < .004$). Truijers et al. used different FEA generating software to compare wall stress in asymptomatic, symptomatic, and ruptured AAAs with size matched external AAA diameters.[24] If homogenous blood pressure values among subgroups were estimated, PWS did not differ significantly. In the present study population the same blood pressure values were estimated for asymptomatic and symptomatic AAAs. Venkatasubramaniam published a comparative study of ruptured and non-ruptured AAAs with standardized blood pressure values.[23] Intact aortic wall properties were assumed for ruptured AAAs. PWS values were significantly higher in ruptured AAAs and rupture sites detected from FEA (i.e. regions of lowest wall stress) accorded to radiologic rupture sites (contrast medium extravasation) from CTA.

Table 2. Biomechanical parameters from FEA of AAA subgroups.

	Asymptomatic AAAs ($n = 30$)	Symptomatic AAAs ($n = 15$)	Ruptured AAAs ($n = 15$)
Peak wall stress (in kPa)	202 ± 34 (138–253)	222 ± 84 (158–511)	317 ± 69 (213–413)
Peak wall rupture risk index	0.46 ± 0.11 (0.27–0.73)	0.62 ± 0.22 (0.41–1.36)	0.83 ± 0.48 (0.51–2.01)
Max AAA diameter (in mm)	59 ± 10 (50–89)	65.3 ± 19 (43–127)	84 ± 18 (66–134)
Total AAA lumen volume (in cm^3)	93 ± 33 (37–160)	118 ± 57 (58–289)	144 ± 122 (66–358)
Volume of intraluminal thrombus (in cm^3)	67 ± 72 (16–327)	71 ± 193 (13–800)	134 ± 96 (6–401)
Rupture risk equivalent diameter (in mm)	53 ± 10 (42–76)	68 ± 18 (49–124)	84 ± 38 (61–178)

Median values ± standard deviation, (lowest-highest values) are shown.

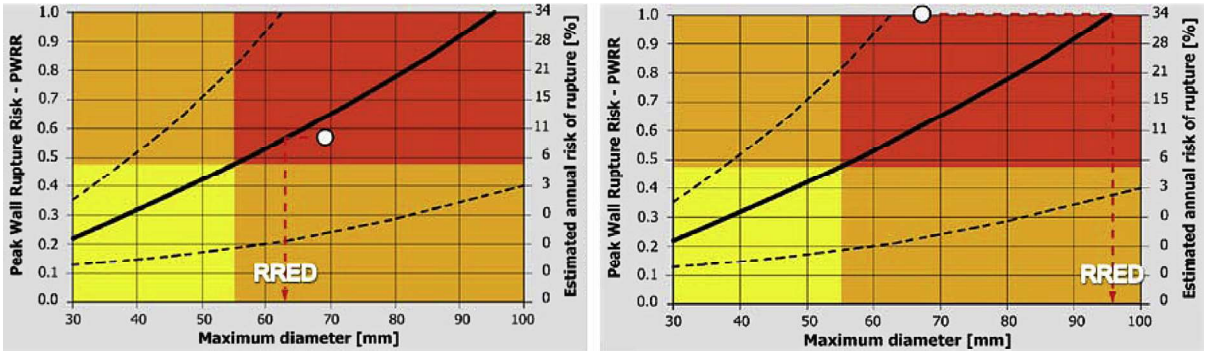

Figure 2. Comparison of an asymptomatic (left panel) and symptomatic AAA (right panel) after FEA. Both external AAA diameters are comparable in diameter (approx. 68 mm, white dots). FEA, however, revealed a significantly increased PWRI (y axis) for the symptomatic AAA. If the PWRI is translated into the "average AAA patient" population (black solid line), RRED is derived. With the consideration of biomechanical parameters, the asymptomatic AAA corresponds to an "average AAA" of 62 mm and the symptomatic AAA to an "average AAA" of 96 mm.

FEA analysis of ruptured AAAs may be regarded as critical. Blood pressure values of the ruptured AAA group registered during patient admission might be influenced by pre-hospital therapy. Hypertensive blood pressure values may be expected at time of rupture onset, thus the calculated wall stress may be underestimated. Rupture inevitably reduces pressure within the AAA and as a minimum, changes local wall geometries. Ideally, for ruptured cases the FEA should have been built from CTAs immediately before rupture to minimize these effects. Noticeably, the FEA model does not differentiate a priori between ruptured and non-ruptured AAAs, and each individual region within the AAA wall is analyzed independently, that is without information on whether it belongs to a ruptured or non-ruptured case. Yet, the lowest pressure regions from FEA corresponded to radiological rupture sites of contrast extravasation. It is emphasized that rupture sites are devoid of a vascular wall. Consequently PWS and PWRI were located distant from rupture sites. From this study it cannot be determined whether maximal wall stress values were located at subsequent rupture sites, as no pre-rupture CTAs were available.

PWRI in this FEA model incorporates most patient specific risk factors and is believed to be the most reliable parameter for AAA rupture risk prediction.[11] These preliminary results suggest that a PWRI >1.0 means rupture in certain individuals and a PWRI >0.5 may identify asymptomatic patients who will become symptomatic or even

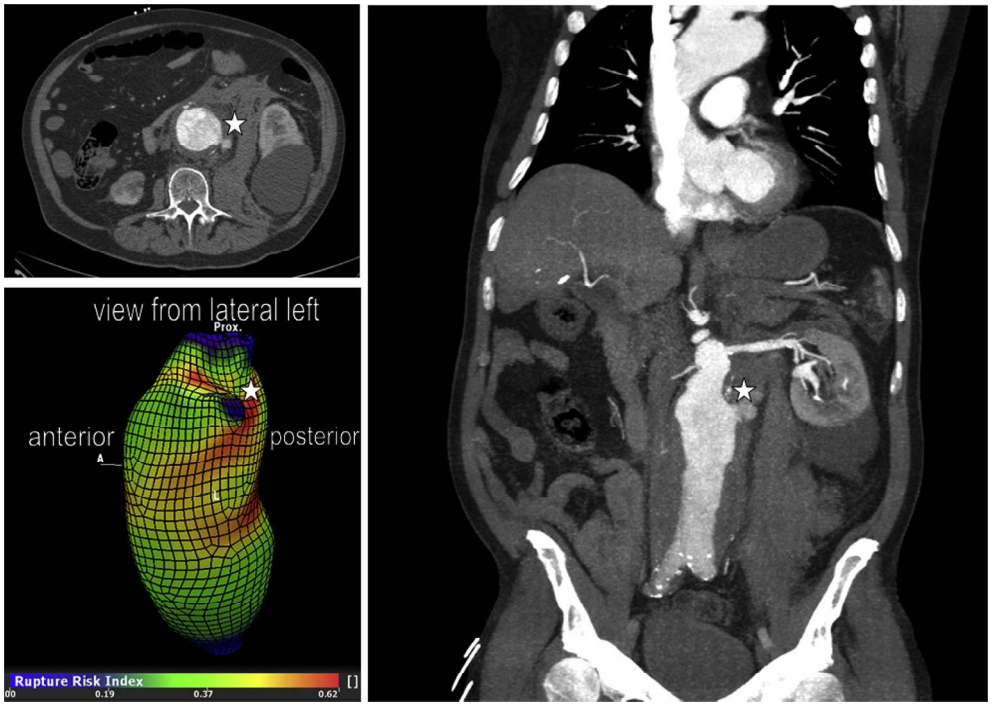

Figure 3. FEA of a ruptured AAA with contrast extravasation. The rupture site was infrarenal and on the left lateral portion of the aneurysm (asterisk). FEA analyzing software precisely identified the rupture location. This region was devoid of vessel wall; therefore local rupture risk was zero (blue color). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

rupture. PWRI calculation is based on standard wall strength properties from elective patients.[11] Biological diversity inevitably influences this parameter. It is assumed that the "watchful waiting" strategy for asymptomatic AAAs may benefit from FEA, even though FEA follow up studies are missing. Manual image processing, 3D rendering, and wall stress calculations are complex and time consuming. This semi-automatic FEA model generates an objective reproducible rupture risk profile that may assist clinicians and patients in clinical decision making. An analyzing workstation can be integrated easily into clinical settings. If connected directly to the radiology server CTA may be analyzed immediately, otherwise data are loaded from external storage devices. Step by step analysis is user friendly and enables prompt biomechanical estimation of AAAs, although FEA is not realizable in all cases.

There are limitations in this study. Selection bias might exist because of consecutive patient recruitment. Multicenter approaches could be used to access a larger study population with comparable AAA and patient characteristics. A further limitation is the assumption of homogenous blood pressure values. The software considers AAA wall properties to be uniform in all patients. Although wall stress is not affected greatly, it is likely that wall strength, and hence PWRI is altered by heterogenous vessel wall properties, for example histopathological degeneration of the AAA vessel wall.[25–27] From histological analysis it is estimated that, even within the same AAA, heterogenous wall properties are coexistent that might influence biomechanics.[28,29]

Although there are study limitations, this FEA model retrospectively yielded biomechanical differences between asymptomatic, symptomatic, and ruptured AAAs. FEA for patient specific AAA rupture risk prediction is still not implemented. The authors support the thesis that PWRI and RRED significantly discriminate between asymptomatic and symptomatic AAA patients with comparable external AAA diameters, whereas further studies are needed to introduce a definitive PWRI threshold value to identify asymptomatic patients at increased rupture risk. These findings may have implications for the indications for surgery or follow up of these patients and lead towards a more individualized treatment approach.

Conclusion

The FEA model provides differences between asymptomatic, symptomatic, and ruptured AAAs. PWRI and RRED are the most critical parameters for differentiating between asymptomatic and symptomatic AAA patients. Asymptomatic AAAs with increased PWRI values may be at higher risk of becoming symptomatic or even rupturing. Individual AAA rupture risk estimation based on FEA alone is still undetermined; however, these preliminary results provide further success in model verification.

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None.

CONFLICT OF INTEREST

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