Prediction of Rupture Sites in Abdominal Aortic Aneurysms After Finite Element Analysis

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Abstract

Purpose: To associate regions of highest local rupture risk from finite element analysis (FEA) to subsequent rupture sites in abdominal aortic aneurysms (AAA). **Methods:** This retrospective multicenter study analyzed computed tomography angiography (CTA) data from 13 asymptomatic AAA patients (mean age 76 years; 8 men) experiencing rupture at a later point in time between 2005 and 2011. All patients had CTA scans before and during the rupture event. FEA was performed to calculate peak wall stress (PWS), peak wall rupture risk (PWRR), rupture risk equivalent diameters (RRED), and the intraluminal thrombus volume (ILTV). PWS and PWRR locations in the prerupture state were compared with subsequent CTA rupture findings. Visible contrast extravasation was considered a definite (n=5) rupture sign, while a periaortic hematoma was an indefinite (n=8) sign. A statistical comparison was performed between the 13-patient asymptomatic AAA group before and during rupture and a 23-patient diameter-matched asymptomatic AAA control group that underwent elective surgery. **Results:** The asymptomatic AAAs before rupture showed significantly higher PWRR and RRED values compared to the matched asymptomatic AAA control group (median values 0.74 vs 0.52 and 77 vs 59 mm, respectively; $p<0.0001$ for both). No statistical differences could be found for PWS and ILTV. Ruptured AAAs showed the highest maximum diameters, PWRR, and RRED values. In 7 of the ruptured AAAs (2 definite and 5 indefinite rupture signs), CTA rupture sites correlated with prerupture PWRR locations. **Conclusion:** The location of the PWRR in unruptured AAAs predicted future rupture sites in several cases. Asymptomatic AAA patients with high PWRR and RRED values have an increased rupture risk.

Keywords

abdominal aortic aneurysm, aneurysm rupture, finite element analysis, intraluminal thrombus, rupture prediction, wall stress

Introduction

Risk stratification and prediction of rupture in abdominal aortic aneurysms (AAA) remain critical issues. The mortality of ruptured AAAs in Western societies ranges from 70% to 90%.[1] The indication for AAA surgical repair is mainly based on the annual expansion rate and maximal diameter of the asymptomatic aneurysm. However, in many cases, both these criteria might over- or underestimate the individual rupture risk. The biomechanical analysis of AAAs using the finite element analysis (FEA) to reconstruct 3-dimensional AAA morphology and calculate biomechanical parameters might describe patient-specific rupture risk more precisely.[2] We have previously reported the biomechanical differences of asymptomatic, symptomatic, and ruptured AAAs and pronounced histological degradation of the aortic wall in high wall stress regions.[3,4] FEA computation incorporates patient-specific risk factors such as hypertension,[5] geometric AAA shape,[6] gender,[7,8] smoking history,[9] and the amount of intraluminal thrombus.[10] Several studies suggest that the peak wall rupture risk (PWRR) index is slightly better than peak wall stress

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Table 1. Patient and FEA Characteristics.[a]

		Rupture Group (n=13)	
	Asymptomatic Group (n=23)	Prerupture Stage	Rupture Stage
Patient characteristics			
Age, y	71 [59–86]	74 [58–81]	76 [58–81]
Men	23	8	
Hypertension	22	13	
Smoking history	13	8	
Coronary heart disease	9	2	
Dyslipidemia	9	6	
Diabetes	3	3	
Renal insufficiency	1	3	
Peripheral occlusive disease	1	2	
FEA characteristics	(n=23)	(n=13)	(n=11)
Peak wall stress, kPa	223 [145–308]	242 [166–384]	297 [211–351]
Peak wall rupture risk index	0.5 [0.3–0.7]	0.7 [0.4–1.1]	0.9 [0.6–1.6]
Maximum AAA diameter, mm	65 [61–89]	65 [56–91]	81 [64–106]
ILTV, cm^3	112 [26–327]	99 [38–238]	134 [51–310]
RRED, mm	59 [37–76]	77 [52–100]	90 [68–148]
RR-systolic during CTA, mm Hg	130 assumed	130 assumed	100 [80–135]
RR-diastolic during CTA, mm Hg	80 assumed	80 assumed	60 [40–100]

Abbreviations: AAA, abdominal aortic aneurysm; FEA, finite element analysis; ILTV, intraluminal thrombus volume; RR (Riva-Rocci), arterial blood pressure; RRED, rupture risk equivalent diameter.
[a]Continuous data are presented as the means [range]; categorical data are given as the counts.

(PWS) in discriminating between intact and ruptured AAAs.[2,3]

The aim of this study was to compare prerupture biomechanics from asymptomatic AAA patients with their subsequent rupture site characteristics. The biomechanical variables were compared between the rupture group and a diameter-matched group of asymptomatic AAA patients without rupture undergoing elective surgery.

Methods

Patients

Thirteen patients (mean age 76 years; 8 men) with initially asymptomatic infrarenal AAAs experiencing rupture at a later point in time between 2005 and 2011 were retrospectively collected from 3 vascular departments [Heidelberg (n=7), Stockholm (n=4), and Nieuwegein (n=2)]. For all patients, computed tomography angiography (CTA) data were present both before and during the rupture event. Median time from prerupture to rupture CTA investigation was 308 days (range 2–2009). Maximum aortic diameter at the time of prerupture CTA detection was above the threshold for surgical intervention (mean 65.2 mm, range 55.5–90.8), but none of the patients underwent surgical intervention until rupture because of endovascular aneurysm repair (EVAR) planning (5), multimorbidity (4), unknown (3), or patient decision (1). Emergency treatment was open surgical repair in 8 and EVAR in 3; perioperative mortality was 45% (5/11 patients). Two patients died before treatment could be initiated.

A control group of 23 consecutive, asymptomatic AAA patients from the vascular department of Heidelberg was chosen for comparison of biomechanical differences with the prerupture stage in the rupture patients; all control patients had undergone elective EVAR or open repair between the years 2012 and 2014. The AAA diameter of the control group was matched (>60 mm) to the prerupture stage of the rupture group. The study was approved by the local medical ethics committee. Patient characteristics are summarized in Table 1.

Finite Element Analysis

FEA was performed by a single investigator using the FEA software A4clinics (Research Edition; VASCOPS GmbH, Graz, Austria). DICOM (Digital Imaging and Communication in Medicine) data from CTAs (in-plane resolution 0.33 mm, slice thickness 0.7–3.3 mm) were used in all cases to reconstruct AAA vessel morphology between the renal arteries and the iliac bifurcation and as a basis for subsequent biomechanical computation. Details regarding FEA generation and image segmentation have been reported.[11] The software provides a high inter- and intrapersonal reproducibility in deriving biomechanical parameters.[12,13]

PWS (in kPa), PWRR, maximum AAA diameter, intraluminal thrombus volume, and rupture risk equivalent diameter

Table 2. Comparison of PWRR Index and PWS Locations With Subsequent CTA Rupture Sites.

Patient	PWS Location	PWRR Location	PWRR Value	Time to Rupture, d	Rupture Sign[a]	CTA Rupture Location	PWRR = Rupture Site?
1	Dorsal infrarenal	Dorsal lateral left	0.8	11	Definite	Dorsal lateral left	Yes
2	Dorsal infrarenal	Dorsal infrarenal	1.1	2	Definite	Lateral right	No
3	Lateral right	Lateral right	0.6	591	Indefinite	Lateral right	Yes
4	Lateral left	Lateral left	0.8	216	Indefinite	Lateral right	No
5	Dorsal	Lateral left	0.8	154	Indefinite	Lateral left	Yes
6	Lateral right	Lateral right	0.7	1100	Indefinite	Lateral left	No
7	Dorsal lateral left	Dorsal lateral left	0.7	2009	Indefinite	Lateral left	Yes
8	Dorsal lateral left	Lateral right	0.6	308	Indefinite	Lateral right	Yes
9	Dorsal proximal bif	Lateral left	0.9	316	Indefinite	Lateral left	Yes
10	Dorsal	Dorsal lateral right	0.9	673	Definite	Lateral left	No
11	Dorsal lateral right	Dorsal lateral left	0.6	383	Definite	Dorsal lateral left	Yes
12	Lateral right	Lateral right	0.4	85	Indefinite	Lateral left	No
13	Dorsal	Dorsal	0.7	49	Definite	Lateral right	No

Abbreviations: bif, iliac bifurcation; CTA, computed tomography angiography; PWRR, peak wall rupture risk index; PWS, peak wall stress.
[a]Definite: contrast medium extravasation on CTA; indefinite: periaortic hematoma on CTA.

(RRED) were calculated in each group. As reported before,[14] the RRED translates the biomechanical profile into the maximum diameter of an "average AAA" with the same risk of rupture (ie, the same PWRR). PWS computation was based on AAA geometry and blood pressure values of the patient, whereas the PWRR (PWS/wall strength) additionally incorporated gender and intraluminal thrombus load. In the prerupture stage of the rupture group and the asymptomatic control group, a systemic blood pressure of 130/80 mm Hg was assumed for biomechanical analysis. For the ruptured AAAs, actual blood pressure values recorded during emergency admission were considered.

PWRR and PWS values in the prerupture stage were compared with the corresponding later CTA rupture sites (Table 2). Visible contrast extravasation was considered a definite rupture site, while periaortic localization of hematoma without signs of contrast extravasation was interpreted as an indefinite rupture site.

Statistical Analysis

Biomechanical parameters (aneurysm diameter, blood pressure, PWRR, RRED, and intraluminal thrombus volume) were compared among the prerupture and rupture stages of the rupture group and the asymptomatic AAA group using the Wilcoxon Mann-Whitney test; $p<0.05$ was considered the threshold for statistical significance. Statistical analyses were performed using Graph Pad Prism (version 4; GraphPad Software, Inc.; La Jolla, CA, USA).

Results

FEA computation was performed for the rupture group (n=13, multicenter data) in both prerupture and rupture stages and for the asymptomatic control group (n=23, single-center data). In two cases from the ruptured stage, vessel reconstruction failed due to massive contrast extravasation, hence FEA computation was possible in 96% of all cases.

Prerupture FEAs were compared with their corresponding rupture CTAs in all 13 cases (Table 2). PWS locations in the prerupture stage correlated to 2 among 8 indefinite rupture sites and to none of the 5 definite rupture sites. The PWRR locations predicted subsequent rupture sites in 2 among the 5 definite and 5 among the 8 indefinite rupture sites (Figures 1 and 2). In 1 of the remaining 3 cases, PWRR location on the prerupture CTA was in the same transversal section with the subsequent definite rupture site. Concordance of the PWRR location and the subsequent rupture site was not based on the time interval between the CTA investigations (Table 2).

Maximal aortic diameters of the asymptomatic control group were matched to the prerupture stage (median 65.2 vs 65.2 mm; p=0.962) of the rupture group. In ascending order, the PWS, PWRR, and RRED values were increased over the asymptomatic AAA control group (Figure 3), while blood pressure values were equal. Specifically, PWRR and RRED values were significantly higher ($p<0.001$) in the prerupture stage compared with the controls (median 0.74 vs 0.52 and 77 vs 59 mm, respectively). No statistical difference in the prerupture and rupture event stages was found for PWS and intraluminal thrombus load [241.7 vs 222.7 kPa (p=0.1) and 99.2 vs 111.6 cm^3 (p=0.695)]. During the time between the prerupture CTA and the rupture event CTA, maximal AAA diameters increased significantly (65.2 vs 80.9 mm; p=0.011). Again, only PWRR and RRED values differed significantly and were higher at the rupture stage compared to the prerupture stage, respectively [0.91 vs 0.74 (p=0.004) and 89.6 vs 76.9 mm (p=0.004)].

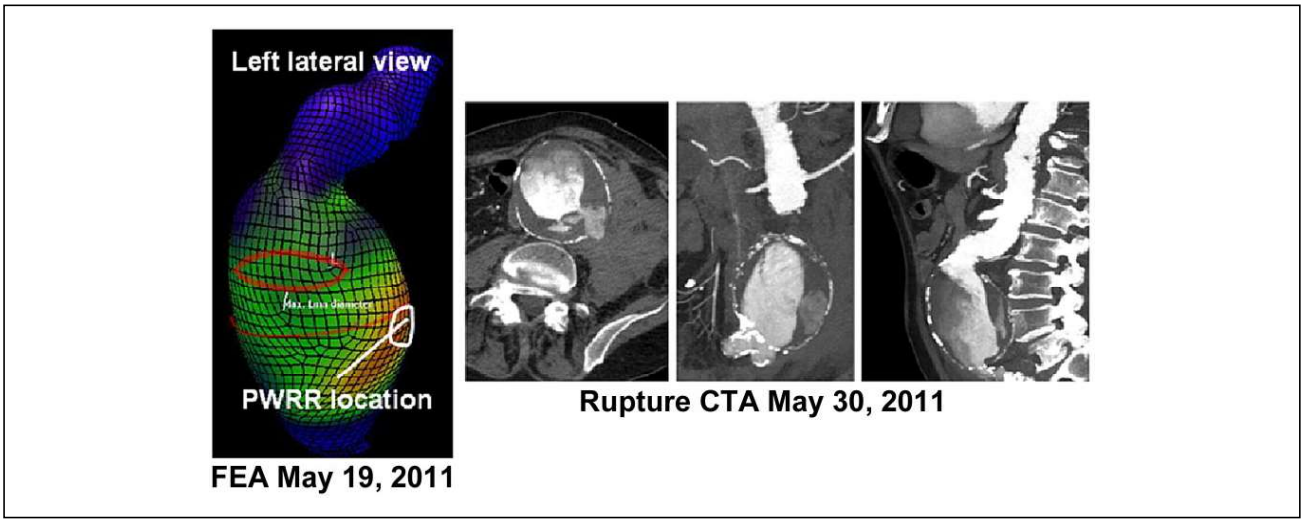

Figure 1. Peak wall rupture risk (PWRR) predicts subsequent definite rupture site. Finite element analysis (FEA, left) of patient 1 indicates PWRR location on the dorsal left lateral region within the aneurysm wall. Eleven days after FEA computation, the aneurysm ruptured (images on the right) and contrast extravasation was detected congruent with the PWRR location. CTA, computed tomography angiography.

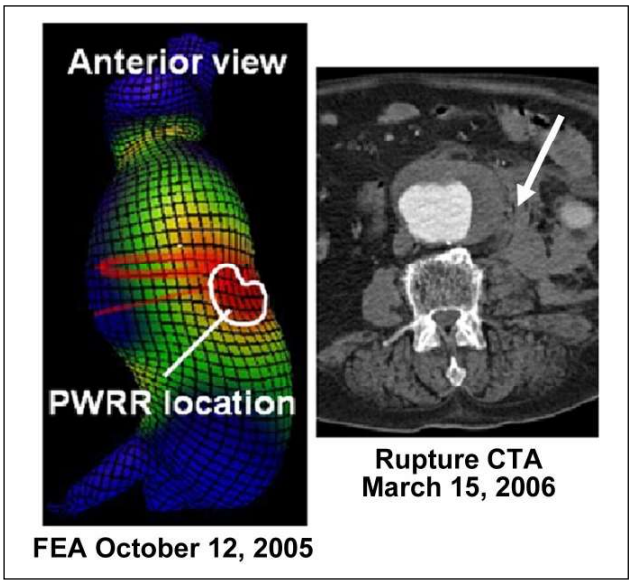

Figure 2. Peak wall rupture risk (PWRR) predicts subsequent indefinite rupture site. Finite element analysis (FEA, left) of patient 5 indicates PWRR location on the left lateral region within the aneurysm wall. Rupture occurred (image on the right) 154 days after FEA computation and a left lateral periaortic hematoma (white arrow) was detected. CTA, computed tomography angiography.

Discussion

In this study, FEA complemented AAA rupture risk assessment. Previous FEA and PWRR identification could predict future rupture site locations in half of the initially asymptomatic AAA patients. The prerupture stage in the ruptured AAA group had higher PWRR and RRED values compared to asymptomatic patients with comparable AAA diameters undergoing elective surgery. So far, no study has been performed to investigate the validity of biomechanical parameters to predict future rupture sites in a high number of asymptomatic AAA cases. Doyle et al[15] recently published a case in which the region of highest AAA wall stress agreed with the future rupture location. Our group recently reported that high rupture risk regions show pronounced histological degeneration compared with low rupture risk regions within the AAA wall.[4] This supports the hypothesis that the location of PWRR might represent regions with the highest biomechanical load leading to focal AAA wall disruption causing rupture. A PWRR value of 1.0 means rupture, in theory, since wall stress exceeds wall strength in an average AAA wall specimen.

Until now, no biomechanical threshold value identifies asymptomatic AAAs that will become symptomatic or even rupture. We recently suggested that a PWRR value between 0.5 and 1.0 should be considered for further validation, and a PWRR >0.5 may identify asymptomatic patients at rupture risk.[3] This could be confirmed by the PWRR results of the prerupture (mean 0.7) and rupture (mean 0.9) stages (Table 1).

We performed a multicenter analysis in order to enlarge our study population of prerupture AAAs with subsequent CTA rupture signs. Identification of definite AAA rupture sites from CTA is restricted in general. Contrast extravasation during the event of AAA rupture is rare and if too pronounced hinders AAA vessel reconstruction and FEA computation. As reported before, the FEA method does not a priori differentiate among ruptured and intact AAAs[3];

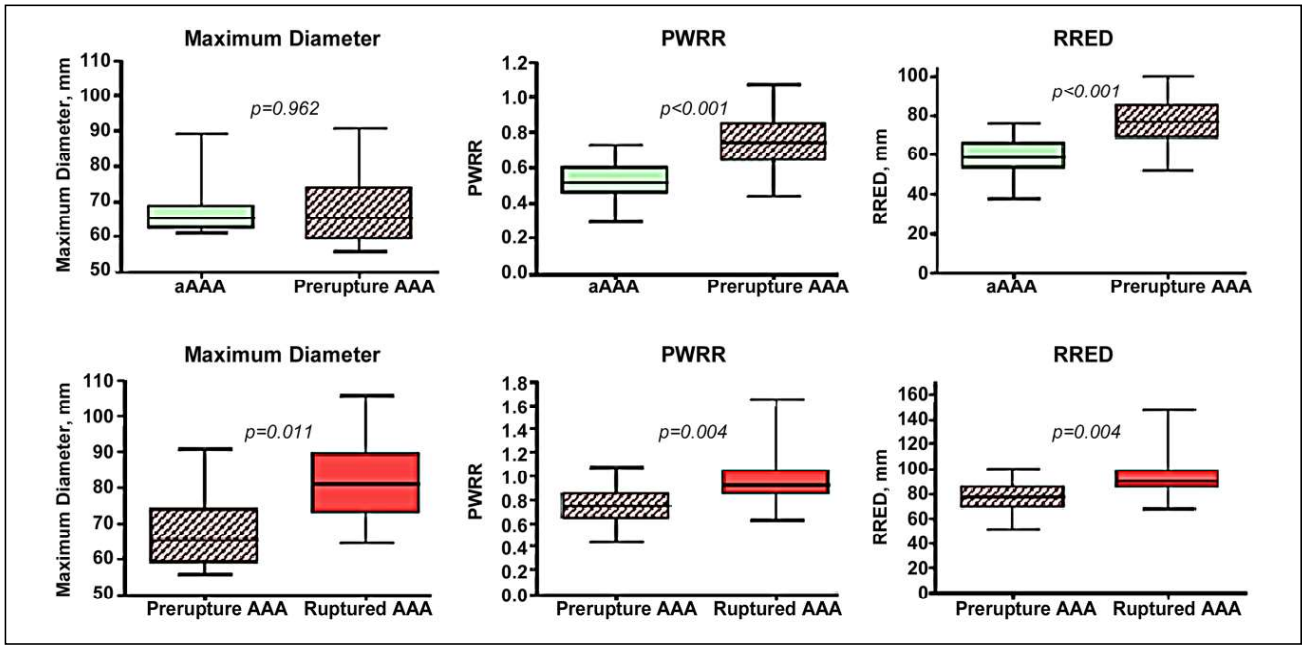

Figure 3. Comparison of biomechanical variables for all subgroups. Compared with the diameter-matched asymptomatic abdominal aortic aneurysm control group (aAAA), the prerupture AAA showed significantly increased peak wall rupture risk (PWRR) and rupture risk equivalent diameter (RRED) values. Comparing the AAA before and after rupture, maximum aortic diameters, PWRR, and RRED were all increased significantly.

thus, a biomechanical comparison between the preruptured and corresponding ruptured AAA is meaningful.

The most common radiologic rupture sign in CTA is the presence of an adjacent hematoma within the retroperitoneal space.[16] Other than the extraluminal rupture signs (contrast extravasation, periaortic stranding/hematoma), there are intraluminal rupture signs (thrombus fissuration, focal wall discontinuity) that have not been considered in this study. Here, we exclusively compared rupture risk profiles in AAAs >50 mm. Rupture risk evaluation in small aneurysms, that is, maximal aortic diameters <50 mm, remains to be investigated in further trials.

As reported earlier,[2] PWRR more precisely discriminates among intact and ruptured AAAs than PWS. For the first time, this analysis demonstrated that PWRR also differentiates most accurately among prerupture AAAs, their corresponding ruptured stage, and asymptomatic diameter-matched AAA individuals. In contrast to PWS location, the region of PWRR predicts subsequent rupture sites more precisely. According to our estimation, biomechanical predictability of subsequent rupture sites was not influenced by the length of time from the prerupture CTA until the rupture event.

No significant differences in global thrombus load were found among the subgroups. The FEA software employed in this study determines the total amount of intraluminal thrombus load. It should be emphasized that differences in local thrombus thicknesses within the AAA wall might exist among the 3 subgroups.

A limitation of the study is the interpretation of indefinite rupture sites (periaortic hematoma). In cases of left lateral retroperitoneal hematoma, we excluded right lateral AAA rupture and vice versa. However, in contrast to definite rupture sites, rupture location estimation in indefinite rupture cases is imprecise.

It is important to note that maximal AAA diameters increased significantly from the time of AAA detection (prerupture stage) to the rupture event. It cannot be answered from this study whether rupture might have occurred in the diameter-matched control group if a conservative approach had been chosen. Biomechanical follow-up studies from patients under the "watchful waiting" strategy are needed to determine relevant parameters causing rupture.

Despite the chosen multicenter approach, the quality of the CTAs was considered comparable. The asymptomatic AAA control group consisted of only male patients. To realize a more detailed matching of study populations (age, gender, AAA diameter, comorbidities), more aortic centers must be recruited for the study.

FEA computation and comparison of PWRR location with subsequent rupture sites was performed by a single investigator. We previously reported that intra- and interindividual reproducibility of deriving FEA parameters was high.[13] An additional study with multiple investigators could achieve consensus on FEA calculations and interpretation of rupture sites.

A further limitation of the study is the assumption of homogenous blood pressure values for the prerupture and asymptomatic AAA groups. In ruptured AAA, blood pressure emergency protocols were available for FEA computation. Despite lower blood pressure values (mean 100/60 mm Hg), the ruptured AAA stage showed the highest biomechanical load as compared with the other subgroups, which is mainly ascribable to the aortic diameter. The recorded blood pressure values, however, do not necessarily reflect blood pressure values at rupture onset and may have been influenced by prehospital emergency medication.

Conclusion

The applied FEA model may provide a more patient-specific AAA rupture risk assessment, but it is debatable whether FEA alone can precisely predict subsequent AAA rupture locations. PWRR and RRED calculations, however, offer promising evidence for general rupture risk stratification in asymptomatic AAA patients.

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