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Estimation of Abdominal Aortic Aneurysm Rupture Risk with Biomechanical Imaging Markers

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ABSTRACT

Purpose: To evaluate whether the biomechanical marker known as rupture risk equivalent diameter (RRED) was superior to the actual abdominal aortic aneurysm (AAA) diameter in estimating future rupture risk in patients who had undergone pre-rupture computed tomography (CT) angiography.

Materials and Methods: A retrospective study was conducted in 13 patients with ruptured AAAs who had undergone CT angiography before and after rupture between 2001 and 2015. The median time between the 2 scans was 731 days. Biomechanical and geometrical markers such as maximal AAA diameter, peak wall stress (PWS), and RRED were calculated with AAA-dedicated software. The main analyses determined whether RRED was higher than the actual diameter and the threshold diameter for elective surgery (55 mm for men, 50 mm for women) in AAAs before and after rupture. Differences between diameter and biomechanical markers before and after rupture were tested with appropriate statistical tests.

Results: RRED before and after rupture was smaller than the actual diameter in 7 of 13 cases. Post-rupture RRED was estimated to be smaller than the threshold diameter for elective repair in 4 cases, again suggesting a low rupture risk. The median PWS before and after rupture was 181.7 kPa (interquartile range [IQR], 152.1–244.2 kPa) and 274.1 kPa (IQR, 172.2–377.2 kPa), respectively.

Conclusions: RRED was smaller than the actual diameter in more than half of pre-rupture AAAs, suggesting a lower rupture risk than estimated with the actual diameter. The results suggest that the currently available biomechanical imaging markers might not be ready for use in clinical practice.

ABBREVIATIONS

AAA = abdominal aortic aneurysm, FEA = finite element analysis, ILT = intraluminal thrombus, IQR = interquartile range, PWRR = peak wall rupture risk, PWS = peak wall stress, RAAA = ruptured abdominal aortic aneurysm, RRED = rupture risk equivalent diameter

Aneurysmal wall biomechanics have been studied extensively in the search for predictors of abdominal aortic aneurysm (AAA) rupture (1). From a biomechanical perspective, an AAA ruptures when hemodynamic forces on the aortic wall exceed aortic wall strength (2,3). Well-known biomechanical imaging markers include peak wall stress (PWS), peak wall rupture risk (PWRR), wall shear stress, and many more (1). Biomechanical markers such as PWS and PWRR can be calculated using finite element analysis (FEA), which is a computational method

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Figure E1 and Tables E1–E4 can be found by accessing the online version of this article on *www.jvir.org* and clicking on the Supplemental Material tab.

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that uses 3-dimensional models of the AAA geometry that are generally obtained from computed tomography (CT) angiography images (1,4,5). PWS calculations are based on the geometry of this 3-dimensional model, wall properties, and blood pressure. When PWS is combined with the estimated wall strength and other patient-specific properties, the rupture risk (or PWRR) can be estimated. Despite the fact that these markers can be easily obtained from standard (contrast-enhanced) CT angiography images, they are currently not applied in the management of patients with AAAs. However, these markers can be easily obtained in clinical practice since CT angiography is frequently carried out in patients with AAA. CT angiography is currently the gold standard for preoperative planning and is also the prime diagnostic modality to detect AAA rupture.

A new and more intuitive marker is the rupture risk equivalent diameter (RRED). RRED is directly derived from PWS and PWRR and expresses rupture risk in diameters (mm) rather than in pressure (kPa) or a risk index. RRED enables an easy comparison of rupture risk with the actual diameter. RRED is the translation of PWRR into the size of an "average" aneurysm that has the same PWRR. This translation is based on a previous cohort study that determined the average rupture risk at different AAA diameters (6).

Previous studies suggested that the mentioned biomechanical markers can differentiate between high and low rupture risk and should be included as an additional marker when considering elective AAA repair (6,7). However, the results and recommendations are predominantly based on case control studies that have compared ruptured AAAs (RAAAs) with intact AAAs. These studies showed that the markers are higher in RAAAs than in asymptomatic AAAs (1,7,8). The results of these case control studies have not been validated in longitudinal studies within the same patients, because only few patients experience rupture after CT angiography imaging of the AAA. Generally, patients undergo CT angiography at a late stage when elective surgery is considered.

Moreover, some previous studies used AAA models after rupture to calculate biomechanical markers for rupture risk prediction. However, the use of images after rupture for this purpose is questionable, as it is unknown whether the rupture itself influences AAA geometry and its corresponding biomechanical markers (1). In addition to the rupture, both hypotension and counter pressure from the retroperitoneal space could cause changes in AAA geometry.

The primary aim of this explorative study was to assess whether FEA-derived biomechanical markers are superior to the actual AAA diameter in estimating future rupture risk. The secondary aim was to compare the characteristics of AAAs before rupture with those of AAAs after rupture to determine whether geometry and biomechanics after rupture are representative of the state before rupture.

MATERIALS AND METHODS

Study Design

This retrospective cohort study followed the STROBE Statement for observational studies (9). The institutional review board of 1 of the participating hospitals waived formal ethical approval for this retrospective study as it was not under the scope of the national law on medical scientific research. Patient informed consent was not required. All clinical information and CT angiography images of patients were coded prior to analysis.

Patients

Patients were identified from 2 academic hospitals: Amsterdam UMC, University of Amsterdam and University Medical Center Groningen. The patients from the first hospital consisted of consecutive patients who presented with RAAAs between 2004 and 2015. These patients were identified from a prospectively maintained RAAA database and a database with insurance codes for patients with RAAAs. The patients from the latter hospital were identified from a prospectively maintained database of patients treated for RAAAs between 2001 and 2014. Patients were eligible for inclusion if they suffered an RAAA and a CT angiography of the AAA before and after rupture (before repair) was available. Rupture of AAA was defined as hemorrhage outside the aortic wall on CT angiography. Patients with a pending rupture or an inflammatory AAA were not included. Patients were also excluded when CT angiography images did not include the total AAA, or when intraluminal contrast delivery was insufficient to segment the aortic lumen for 3-dimensional mesh generation.

Twenty patients with CT scans before and after rupture were identified. Seven patients were excluded because FEA could not be carried out in 10 scans (**Fig 1**). The AAA was not fully captured in 2 pre-rupture scans; arterial contrast was not administered in 1 scan before rupture and 2 scans after rupture; arterial contrast delivery was insufficient in 1 scan before rupture and 1 scan after rupture; contrast extravasation was massive in 1 scan after rupture; and segmentation errors occurred in the before and after rupture scans of 1 patient.

Thirteen patients were included in the analysis. Seven of 13 patients were male, and age at rupture ranged from 65 to 87 years (median, 71.0 years). The time interval between the 2 scans ranged from 106 days to 7.4 years (median, 731 days). Other patient characteristics are listed in **Table E1** (available online on the article's Supplemental Material page at *www.jvir.org*). Eight patients had a pre-rupture diameter larger than the repair threshold. Reasons for the fact that these patients had not undergone elective repair were the following: 6 patients had substantial comorbidity (4 were ineligible for endovascular aneurysm repair [EVAR]; 1 patient was scheduled for elective repair, but the AAA ruptured prior to the operation date; and 1 AAA was measured as smaller than the threshold diameter by the radiologist. Ruptured AAAs were treated by open repair in 7

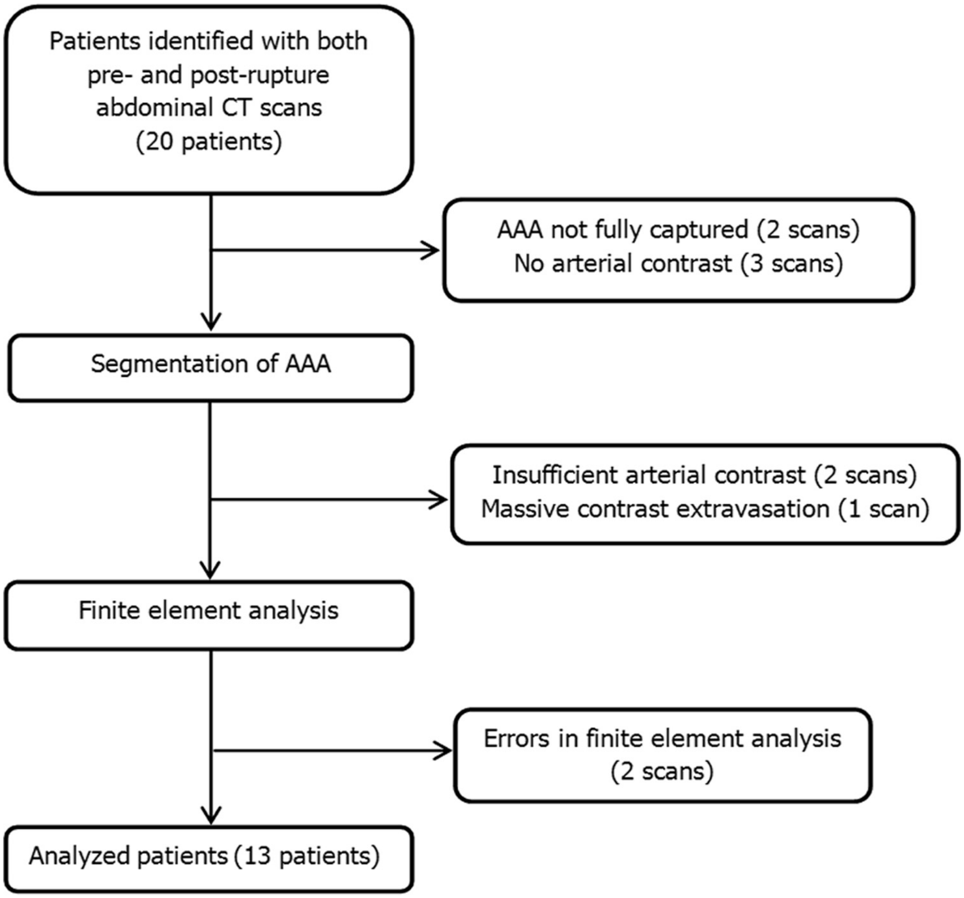

Figure 1. Flowchart of analysis process.

and by EVAR and palliative management in 3 each (**Table E1** [available online on the article's Supplemental Material page at *www.jvir.org*]). Clinical blood pressure values were unavailable for 2 scans before rupture and 3 scans after rupture.

Segmentation

The entire workflow of segmentation and FEA was carried out with commercially available software dedicated to AAA (A4clinics Research Edition; Vascops GmbH, Graz, Austria). This software was developed for users without skills in computational mechanics or image analysis (10). The segmentation and FEA of each AAA was completed within 30 minutes for most cases. The time needed was mostly dependent on the tortuosity and contrast delivery.

The AAA was segmented from previously obtained CT angiography images. CT angiography was performed using multidetector CT scanners (4–64 slice detectors) of Philips (Best, Netherlands), Siemens (Munich, Germany), or Toshiba (Tokyo, Japan). The reconstructed slice thickness ranged from 0.5 to 5.0 mm (median, 2.5 mm). The segmentation was semi-automatic and was performed by a single investigator (H.J.). The boundaries of the aortic lumen, the intraluminal thrombus (ILT), and the aortic wall were detected automatically and were manually corrected when necessary. Good interobserver and intraobserver agreement was previously demonstrated for segmentation of non-ruptured AAAs (11). To improve the accuracy of the segmentation, a radiologist with 6 years of experience in cardiovascular imaging (R.N.P.) confirmed all segmentations.

FEA

To calculate the biomechanical parameters, the software integrated the geometrical 3-dimensional model of the AAA with mechanical tissue properties (such as elasticity and strength of the AAA wall and ILT) and patient characteristics. Long-term blood pressure was based on results from outpatient files. Post-rupture blood pressure was obtained from emergency department files. When blood pressures were not available in the patient files, the recommended value of 140/80 mmHg was used.

The FEA workflow was almost entirely automated. In short, the geometrical models were first meshed into hexahedral elements (10). Additionally, the software includes some assumptions regarding the aneurysm wall and ILT and incorporates strength and elasticity of the aneurysm wall according to in vitro measurements (12–14). These were implemented in an isotropic constitutive model. The model uses an average wall thickness that variates based on the mean arterial pressure position in relation to the thrombus. This segmentation and meshing algorithm has previously been published in detail (10).

PWS

The calculation of wall stress (and its peak value PWS, expressed in kPa) finds it origin in Laplace's law for wall tension but is more comprehensive and incorporates (among others) AAA size, asymmetry, wall thickness, mechanical wall properties, and arterial pressure.

PWRR

PWRR is calculated by dividing PWS by the wall strength. The wall strength is calculated based on studies with aortic specimens and is also estimated with patient-specific properties such as ILT position and size, sex, and family history for ruptured aneurysms (15–17).

RRED

RRED is a new and more intuitive marker for rupture risk. It is the expression of biomechanical rupture risk into diameter (mm). RRED reflects the average AAA diameter with the same PWRR. This average diameter is based on a previously described reference population of intact AAAs (6). **Figure 2** illustrates how an AAA with an actual diameter of 66 mm could have a RRED of 82 mm when its estimated PWRR corresponds to the PWRR of an AAA of 82 mm.

This study determined whether RRED was higher than the actual diameter in both AAAs before and after rupture. RRED values were also determined in the AAAs after rupture to ascertain that the RRED values demonstrated the high rupture risk. Furthermore, this study determined whether RRED was larger or smaller than threshold diameters for elective surgery (5.5 cm for men and 5.0 cm for women).

Geometrical Parameters

The geometrical parameters were automatically calculated and comprised maximal exterior AAA diameter (mm), luminal AAA diameter (mm), ILT thickness (mm), total vessel volume (cm^3), lumen volume (cm^3), and ILT volume (cm^3). Volumes were measured between the aortic bifurcation and the most distal renal artery for infrarenal AAAs and the superior mesenteric artery for juxtarenal AAAs. Volumes were not included for further analysis when the scan did not involve the total length between the proximal and distal boundary.

Statistical Analysis

Continuous variables are reported as median with interquartile range (IQR). Geometrical and biomechanical parameters are also reported as mean ± standard deviation in the tables. The distribution of data was tested with the Shapiro-Wilk test. The paired *t*-test was used to assess differences between diameter, volume, PWS, and RRED before and after rupture. The Wilcoxon signed-rank test was used to assess the difference between PWRR before and after rupture. A P value of $< .05$ was considered statistically significant. Data were analyzed using IBM SPSS Statistics version 23 (IBM Inc, Armonk, New York).

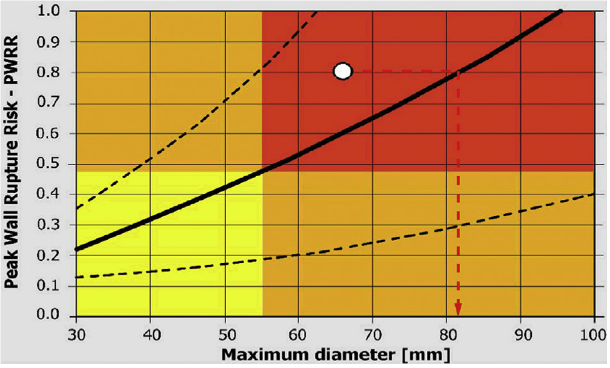

Figure 2. Estimation of the rupture risk equivalent diameter (RRED). The dot represents a patient with a maximal AAA diameter of 66 mm and a PWRR of 0.8. In the mean population (represented by the thick black line), a PWRR of 0.8 corresponds with a maximal AAA diameter of 82 mm, resulting in a RRED of 82 mm. This figure was created with A4clinics Research Edition (Vascops GmbH).

RESULTS

Rupture Risk Estimation before Rupture

RRED was smaller than the actual diameter in 7 of 13 cases (**Fig 3**), thereby demonstrating a lower risk of rupture compared to a rupture risk estimation based on the actual diameter only (**Table E3** [available online on the article's Supplemental Material page at *www.jvir.org*]; Patients 1, 2, 3, 8, 10, 12, and 13).The median pre-rupture RRED was 57.8 mm (IQR, 42.0–78.3 mm). This corresponded with a median PWS of 181.7 kPa (IQR, 152.1–244.2 kPa) and PWRR of 0.51 (IQR, 0.34–0.77) (**Table E4** [available online on the article's Supplemental Material page at *www.jvir.org*]). In comparison, the average PWS of a normal aorta of 20 mm is approximately 77–80 kPa, and the average PWRR is approximately 0.13–0.15 (6).

The RRED of 6 pre-rupture AAAs was below the threshold diameter for elective repair (**Table E3** [available online on the article's Supplemental Material page at *www.jvir.org*]; Patients 1, 2, 3, 10, 12, and 13). However, 5 of the pre-rupture AAAs had a diameter smaller than the threshold diameter (>5.5 cm for men and >5.0 cm for women; Patients 1, 4, 5, 10, and 12).

Post-rupture Rupture Risk Estimation

RRED was estimated smaller than the actual diameter in 7 cases (**Table E3** [available online on the article's Supplemental Material page at *www.jvir.org*]; Patients 1, 2, 3, 9, 10, 12, and 13). RRED was estimated smaller than the threshold

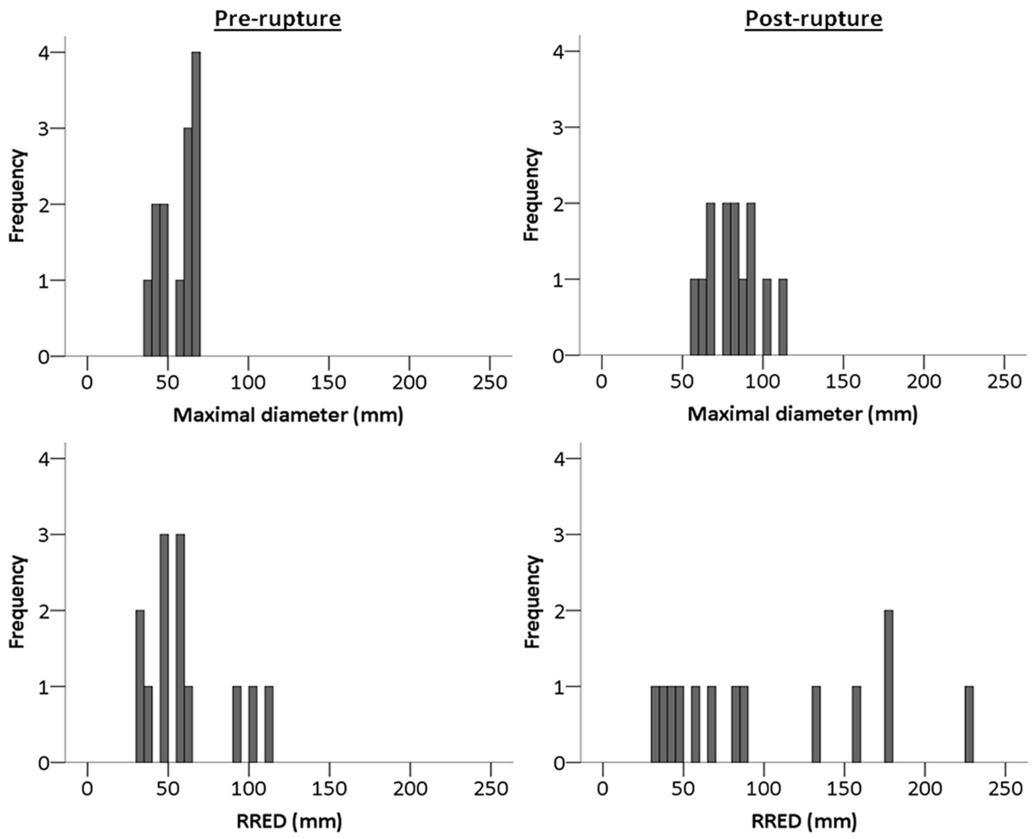

Figure 3. Distribution of maximal diameters and RRED in AAAs before and after rupture. *RRED was smaller than the actual maximal diameter before and after rupture in 7 of 13.

diameter for elective repair in 4 cases (>5.5 cm for men and >5.0 cm for women; **Table E3** [available online on the article's Supplemental Material page at *www.jvir.org*]; Patients 1, 2, 12, and 13). The actual diameter of all AAAs after rupture was >5.5 cm. The median RRED after rupture was 81.4 mm (IQR, 44.6–167.7 mm). This corresponded with a median PWS of 274.1 kPa (IQR, 172.2 –377.2 kPa) and PWRR of 0.80 (IQR, 0.36–1.89) (**Table E4** [available online on the article's Supplemental Material page at *www.jvir.org*]).

Rupture Location

Active contrast extravasation was identified in 9 of 13 scans after rupture (**Table E3** [available online on the article's Supplemental Material page at *www.jvir.org*]). In the remaining 4, rupture was identified by the presence of retroperitoneal hemorrhage outside the aortic wall. Contrast extravasation and hematoma locations are listed in **Table E3** (available online on the article's Supplemental Material page at *www.jvir.org*).

Changes between State before and after Rupture

Geometrical parameters. Differences in geometry before and after rupture are presented in **Figure 4**. Maximal external AAA diameter increased from before and after rupture state in all patients (**Table E3** [available online on the article's Supplemental Material page at *www.jvir.org*]), and maximal lumen diameter increased in 12 of 13 patients. Median maximal diameter before rupture increased from 60.8 mm (IQR, 45.8–67.8 mm) to a median diameter after rupture of 81.2 mm (IQR, 68.5–93.1 mm) ($P < .001$; **Table E4** [available online on the article's Supplemental Material page at *www.jvir.org*]). Growth of the maximal diameter ranged from 3.3 mm/year to 90.6 mm/year (median, 12.3 mm/year; IQR, 7.2–20.4 mm/year; **Table E2** [available online on the article's Supplemental Material page at *www.jvir.org*]). The 2 AAAs with the shortest time interval between scans had the highest growth rate (**Table E2** [available online on the article's Supplemental Material page at *www.jvir.org*]; Patients 2 and 7).

Biomechanical parameters. PWS, PWRR, and RRED increased in 10 patients from state before rupture to after rupture. Median PWS, PWRR, and RRED were significantly higher in the state after rupture than the state before rupture ($P = .006$, .009, and .005, respectively). The PWS location changed between AAAs before and after rupture in 8 patients (**Table E3** [available online on the article's Supplemental Material page at *www.jvir.org*]). The location of PWS varied widely throughout the AAAs, and no predominant PWS location could be identified. The location of PWRR changed between AAAs before and after rupture in 7 patients. The location of PWRR was similar to that of PWS

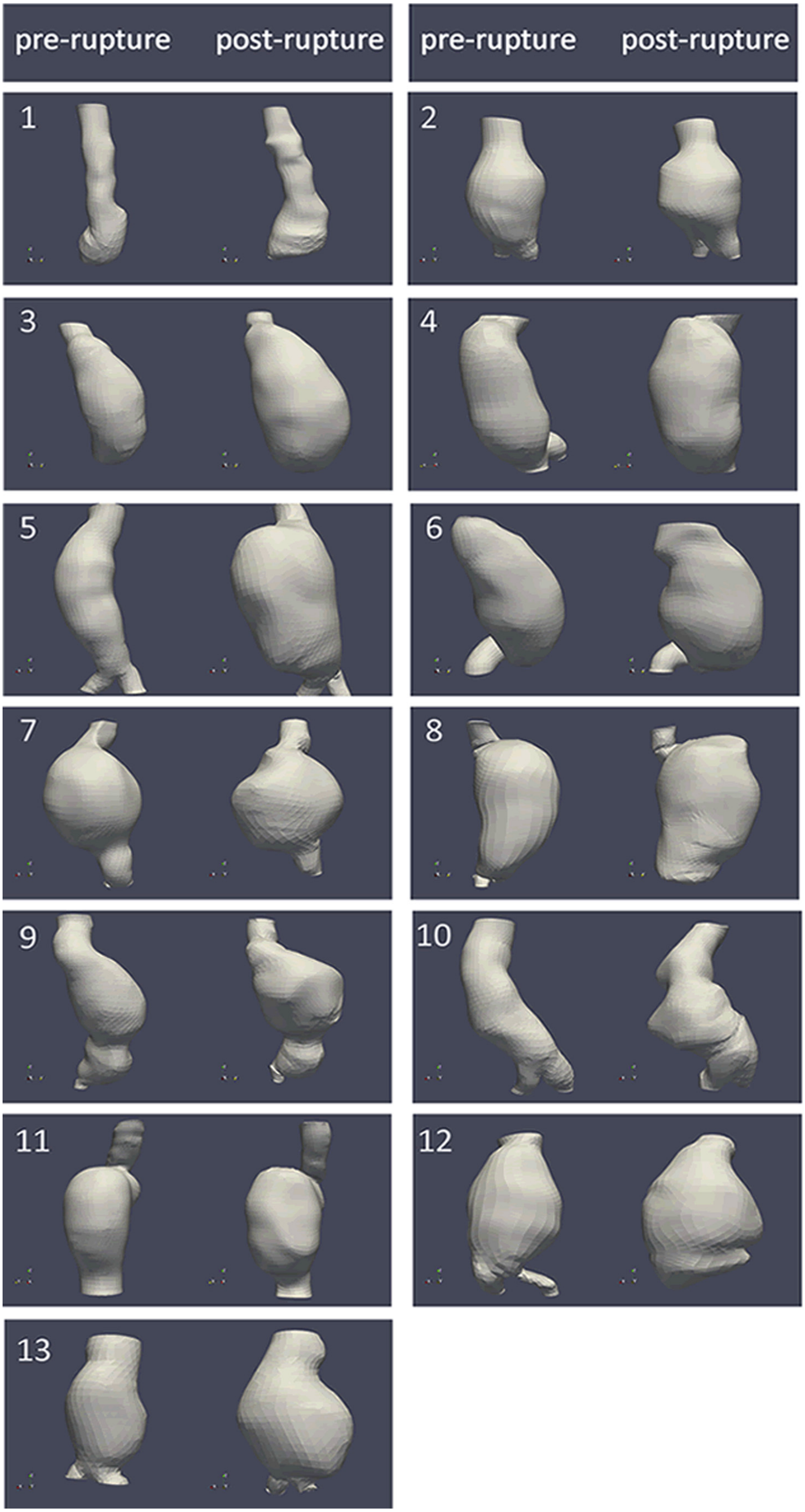

Figure 4. Anteroposterior view of the 3-dimensional segmentations of the CT angiography images before and after rupture. *The diameters and time interval between scans are listed in Table E3 (available online on the article's Supplemental Material page at *www.jvir.org*).

in most AAAs (**Table E3**, **Fig E1** [available online on the article's Supplemental Material page at *www.jvir.org*]).

DISCUSSION

The presented data demonstrate that FEA-derived biomechanical markers currently have limited value in AAA rupture risk stratification. Remarkably, RRED was smaller than the actual diameter in more than half of AAAs before rupture, suggesting a lower rupture risk than estimated with the actual diameter. Furthermore, RRED was smaller than the threshold diameter for elective repair in 4 AAAs that had already ruptured. Moreover, the presented data demonstrate a difference between geometry of AAAs before and after rupture. The higher PWS and PWRR values on scans after rupture likely reflect the effects of aneurysm growth rather than those of aneurysm rupture. However, the changing locations of PWS and PWRR could also suggest a morphologic change as a consequence of rupture.

More than a dozen studies have investigated the biomechanical imaging markers examined in this study (1). The studies found that the markers are higher in RAAA than in asymptomatic AAAs. However, some studies were subject to confounding bias since the analyzed RAAAs had a larger diameter than the asymptomatic AAAs (6,17,18). Therefore, it was to be expected that PWS and PWRR were to be higher in RAAAs compared to asymptomatic AAAs, as PWS and PWRR increase with diameter. Some authors tried to correct for this confounding factor by including patients with matching diameters of RAAAs and asymptomatic AAAs (19). Despite these corrections, several factors still limit the extrapolation of results and the use of the biomechanical markers in clinical rupture risk stratification. First, the results of the case control studies have not been validated in longitudinal studies within the same patients. The results reflect differences between different patients, albeit diameter-matched in some studies. Another limitation is that PWS and PWRR have often been estimated on images after rupture (7,17,20,21). It is unknown whether models after rupture are representative of the pre-rupture state since it is not known to which extent the rupture itself influences AAA geometry and the corresponding biomechanical results.

This study is not the first to report on biomechanical differences between scans before and after rupture. A recent study by Erhart et al (22) compared PWS and PWRR regions with future rupture location in 13 AAAs before and after rupture of the same patients in a case control design. The study also reported that maximal diameter, PWRR, and RRED were significantly higher in AAAs after rupture (22). Before and after rupture outcomes within the same patients with AAA have not been studied before. Availability of both scans of AAAs before and after rupture is scarce since AAA surveillance is generally carried out with duplex ultrasound, and CT angiography scans are typically only performed in a late stage when AAA surgery is considered. However, other studies with intracranial aneurysms have demonstrated the presence of rupture-associated changes (23,24).

A remarkable result of the present study was the high median aneurysm growth rate of 12.3 mm/year between scans before and after rupture. High growth rates were to be expected because of the large sizes of AAAs in this cohort (median pre-rupture diameter was 61 mm). However, the observed growth rates remain very high compared to growth rates reported in the literature (pooled growth rates of 5.0 mm/year for AAAs of 45–49 mm) (25). Even more interestingly, the highest growth rates were observed in the patients with the shortest time interval between scans, and the lowest growth rates were observed in the patients with the longest time interval. It is likely that the high growth rate was the cause of rupture rather than its consequence. Yet it remains unknown whether the AAA mostly expanded in the final stages prior to rupture or linearly across the entire time interval between scans.

The three main limitations of the current study were its retrospective design, the small sample size, and the long time interval between scans before and after rupture. The retrospective design could have introduced selection bias and inadequate reporting of baseline characteristics. Seven of the 20 initially identified patients needed to be excluded in the selection process because segmentation or FEA could not be carried out. As a consequence of the exclusions, almost half of the cohort consisted of females, because 5 of 7 excluded patients were men. In addition, the maximal diameter differed between the included and excluded patients (median, 81 vs 73 mm at rupture). Only 3 of 13 patients had a time interval of less than a year between scans. These small numbers make it difficult to draw firm conclusions on the effects of aneurysm rupture on aneurysm geometry and biomechanics. Partly because of the small sample size, no statistical tests were performed to compare RRED and diameter. This study only assessed whether RRED was higher or lower than the actual diameter. In addition, the time interval between scans made it difficult to determine which changes occurred before, during, or after rupture.

A major limitation of the used FEA technique is that segmentations of especially ruptured AAAs needed manual adjustment of the automatic segmentation. The manual adjustments concerned drawn vessel boundaries and adjustments of standard numerical thresholds and gradients. This is a topic that is not often highlighted in other reports of FEA studies. Furthermore, the segmentation by a single investigator could have caused operator bias.

The results of this study suggest that FEA-derived imaging markers might not be ready to be applied in clinical practice. RRED was smaller than the actual diameter in more than half of pre-rupture AAAs.

Furthermore, the geometry of AAAs after rupture was different from that of pre-rupture AAAs, even though the long time interval between scans prevented accurate determination of which changes occurred before, during, or after rupture. Future studies with larger prospective cohorts of patients with both scans of the AAA before and after rupture are needed to further investigate the currently observed limitations of the FEA method.

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REFERENCES

1. Indrakusuma R, Jalalzadeh H, Planken RN, et al. Biomechanical imaging markers as predictors of abdominal aortic aneurysm growth or rupture: a systematic review. Eur J Vasc Endovasc Surg 2016; 52:475–486.
2. Vorp DA. Biomechanics of abdominal aortic aneurysm. J Biomech 2007; 40:1887–1902.
3. Rodel SGJ, Meerwaldt R, Geelkerken RH, et al. Risk factors for AAA growth and rupture; more than diameter alone. In: de Vries JPPM, editor. *Latest insights into abdominal aortic aneurysms and endovascular repair*. Torino: Edizioni Minerva Medica; 2012. p. 11–26.
4. Leemans EL, Willems TP, van der Laan MJ, et al. Biomechanical indices for rupture risk estimation in abdominal aortic aneurysms. J Endovasc Ther 2017; 24:254–261.
5. Fillinger MF, Raghavan ML, Marra SP, et al. In vivo analysis of mechanical wall stress and abdominal aortic aneurysm rupture risk. J Vasc Surg 2002; 36:589–597.
6. Gasser TC, Nchimi A, Swedenborg J, et al. A novel strategy to translate the biomechanical rupture risk of abdominal aortic aneurysms to their equivalent diameter risk: method and retrospective validation. Eur J Vasc Endovasc Surg 2014; 47:288–295.
7. Erhart P, Hyhlik-Durr A, Geisbusch P, et al. Finite element analysis in asymptomatic, symptomatic, and ruptured abdominal aortic aneurysms: in search of new rupture risk predictors. Eur J Vasc Endovasc Surg 2015; 49:239–245.
8. Khosla S, Morris DR, Moxon JV, et al. Meta-analysis of peak wall stress in ruptured, symptomatic and intact abdominal aortic aneurysms. Br J Surg 2014; 101:1350–1357; discussion 1357.
9. von Elm E, Altman DG, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. J Clin Epidemiol 2008; 61: 344–349.
10. Auer M, Gasser TC. Reconstruction and finite element mesh generation of abdominal aortic aneurysms from computerized tomography angiography data with minimal user interactions. IEEE Trans Med Imaging 2010; 29:1022–1028.
11. Teutelink A, Cancrinus E, van de Heuvel D, et al. Preliminary intraobserver and interobserver variability in wall stress and rupture risk assessment of abdominal aortic aneurysms using a semiautomatic finite element model. J Vasc Surg 2012; 55:326–330.
12. Raghavan ML, Vorp DA. Toward a biomechanical tool to evaluate rupture potential of abdominal aortic aneurysm: identification of a finite strain constitutive model and evaluation of its applicability. J Biomech 2000; 33: 475–482.
13. Vande Geest JP, Sacks MS, Vorp DA. A planar biaxial constitutive relation for the luminal layer of intra-luminal thrombus in abdominal aortic aneurysms. J Biomech 2006; 39:2347–2354.
14. Gasser TC, Gorgulu G, Folkesson M, et al. Failure properties of intraluminal thrombus in abdominal aortic aneurysm under static and pulsating mechanical loads. J Vasc Surg 2008; 48:179–188.
15. Vande Geest JP, Di Martino ES, Bohra A, et al. A biomechanics-based rupture potential index for abdominal aortic aneurysm risk assessment: demonstrative application. Ann N Y Acad Sci 2006; 1085:11–21.
16. Vande Geest JP, Wang DH, Wisniewski SR, et al. Towards a noninvasive method for determination of patient-specific wall strength distribution in abdominal aortic aneurysms. Ann Biomed Eng 2006; 34:1098–1106.
17. Gasser TC, Auer M, Labruto F, et al. Biomechanical rupture risk assessment of abdominal aortic aneurysms: model complexity versus predictability of finite element simulations. Eur J Vasc Endovasc Surg 2010; 40: 176–185.
18. Fillinger MF, Marra SP, Raghavan ML, et al. Prediction of rupture risk in abdominal aortic aneurysm during observation: wall stress versus diameter. J Vasc Surg 2003; 37:724–732.
19. Truijers M, Pol JA, Schultzekool LJ, et al. Wall stress analysis in small asymptomatic, symptomatic and ruptured abdominal aortic aneurysms. Eur J Vasc Endovasc Surg 2007; 33:401–407.
20. Venkatasubramaniam AK, Fagan MJ, Mehta T, et al. A comparative study of aortic wall stress using finite element analysis for ruptured and non-ruptured abdominal aortic aneurysms. Eur J Vasc Endovasc Surg 2004; 28:168–176.
21. Heng MS, Fagan MJ, Collier JW, et al. Peak wall stress measurement in elective and acute abdominal aortic aneurysms. J Vasc Surg 2008; 47: 17–22; discussion 22.
22. Erhart P, Roy J, de Vries JP, et al. Prediction of rupture sites in abdominal aortic aneurysms after finite element analysis. J Endovasc Ther 2016; 23: 115–120.
23. Schneiders JJ, Marquering HA, van den Berg R, et al. Rupture-associated changes of cerebral aneurysm geometry: high-resolution 3D imaging before and after rupture. AJNR Am J Neuroradiol 2014; 35:1358–1362.
24. Cornelissen BM, Schneiders JJ, Potters WV, et al. Hemodynamic differences in intracranial aneurysms before and after Rupture. AJNR Am J Neuroradiol 2015; 36:1927–1933.
25. Powell JT, Sweeting MJ, Brown LC, et al. Systematic review and meta-analysis of growth rates of small abdominal aortic aneurysms. Br J Surg 2011; 98:609–618.

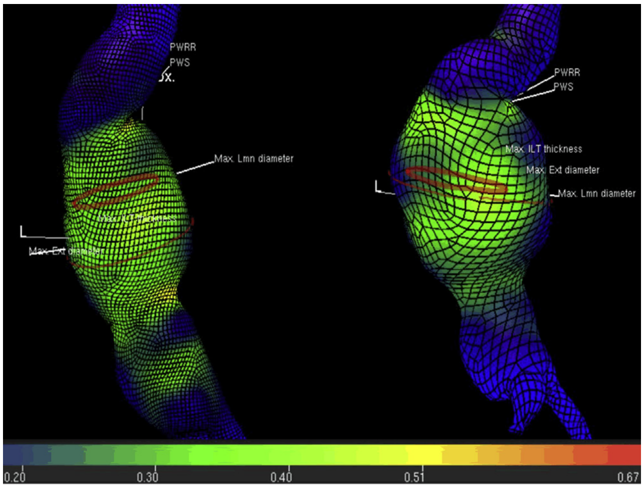

Figure E1. Before and after rupture AAA. The color scale represents the rupture risk index.

Table E1. Patient Characteristics

Patient no.	Age at rupture	Sex	Long-term blood pressure (mmHg)	Blood pressure post- rupture (mmHg)	Smoking	COPD	Diabetes mellitus	Cardiovascular disease *	Hyper-choles-terolemia	Normal infrarenal diameter (mm) †	Treatment for rupture
1	87	Male	150/80	-	yes	yes	no	yes	no	25	EVAR
2	71	Male	140/90	110/60	yes	no	no	no	yes	21	OSR
3	70	Male	130/80	120/75	yes	yes	yes	yes	yes	21	OSR
4	81	Female	140/80	-	yes	no	no	yes	yes	19	Palliative
5	71	Female	160/100	-	yes	no	no	yes	yes	17	OSR
6	65	Female	115/95	156/136	no	no	no	no	no	16	OSR
7	66	Female	140/85	-	yes	yes	no	yes	no	17	EVAR
8	77	Female	-	90/50	yes	yes	no	no	no	18	OSR
9	82	Male	115/75	94/63	yes	no	no	yes	no	23	OSR
10	86	Male	115/90	114/94	yes	yes	no	yes	no	24	Palliative
11	65	Female	165/85	140/85	no	no	no	yes	no	16	OSR
12	67	Male	-	120/80	yes	yes	no	no	no	21	EVAR
13	81	Male	120/85	85/50	yes	no	yes	yes	yes	22	Palliative

COPD = chronic obstructive pulmonary disorder; EVAR = endovascular aneurysm repair; OSR = open surgical repair.
*Cardiovascular disease was defined as: heart disease (myocardial infarction, angina pectoris, congestive heart failure, or prior coronary intervention), cerebrovascular disease (stroke or transient ischemic attack) and peripheral arterial disease (with or without prior revascularization procedure).
†Based on age and sex, estimation by the software.

Table E2. AAA Growth between Scans

Patient No.	Time between scans (years)	Pre-rupture diameter (mm)	Maximal diameter growth (mm)	Maximal diameter growth/year (mm/year)
1	1.31	47.7	16.1	12.3
2	0.34	60.8	8.2	24.0
3	2.51	59.0	25.0	10.0
4	4.73	43.9	37.3	7.9
5	4.85	40.0	27.9	5.7
6	0.97	62.9	15.9	16.3
7	0.29	67.9	26.3	90.6
8	1.16	69.1	20.8	17.9
9	2.00	62.5	38.1	19.0
10	2.48	49.2	27.0	10.9
11	1.95	68.5	42.6	21.8
12	2.64	38.4	17.1	6.5
13	7.41	67.7	24.3	3.3

AAA = abdominal aortic aneurysm.

Table E3. Summary of Geometrical and Biomechanical Results

	Pre-rupture (n = 13)		Post-rupture (n = 13)	
	Median (interquartile range)	Mean ± standard deviation	Median (interquartile range)	Mean ± standard deviation
Ext diameter (mm)	60.8 (45.8 –67.8)	56.7 ± 11.4	81.2 (68.5–93.1)	81.9 ± 15.7
Lumen diameter (mm)	37.0 (30.9–46.0)	39.2 ± 11.7	53.7 (40.2–72.4)	55.3 ± 18.4
ILT thickness (mm)	20.8 (4.4–27.0)	17.7 ± 12.2	27.6 (19.7–36.7)	27.8 ± 9.8
Total volume (cm^3)	128.9 (84.6– 225.6) *	151.4 ± 78.1 *	246.9 (176.4– 388.4) *	279.3 ± 134.3 *
Lumen volume (cm^3)	58.4 (36.0 –66.1) *	57.4 ± 29.8 *	91.9 (53.3–196.6) *	122.0 ± 82.0*
ILT volume (cm^3)	51.0 (18.7– 152.3) *	73.9 ± 69.4 *	108.7 (72.4 – 191.5) *	129.1 ± 70.4 *
PWS (kPa)	181.7 (152.1– 244.2)	196.8 ± 59.1	274.1 (172.2– 377.2)	275.6 ± 121.5
Mean wall stress (kPa)	104.0 (75.6–122.8)	101.1 ± 25.7	109.1 (84.4– 152.0)	120.8 ± 44.9
PWRR	0.51 (0.34–0.77)	0.57 ± 0.32	0.80 (0.36–1.89)	1.07 ± 0.80
RRED (mm)	57.8 (42.0–78.3)	60.9 ± 25.7	81.4 (44.6–167.7)	101.8 ± 65.0

Note–Median PWS, PWRR, and RRED were significantly higher in the post-rupture state compared to the pre-rupture state ($P = .006$, .009, and .005, respectively).
CTA = computed tomography angiography; ILT = intraluminal thrombus; PWRR = peak wall rupture risk; PWS = peak wall stress; RRED = rupture risk equivalent diameter.
*Volume measurements are based on 10 patients. The volume was not measured in 3 patients because the CTA images did not include the entire region from the distal renal artery to the aortic bifurcation.

Table E4. Patient-Specific Geometrical and Biomechanical Results

Patient no.	AAA	Time between scans (years)	Max. external diameter (mm)	RRED (mm)	Total volume (cm^3)	PWS (kPa)	PWS location	Mean WS (kPa)	PWRR	PWRR location	Retroperi-toneal hematoma, predominant location	Visible contrast extra-vasation
1	Asymp-tomatic	-	47.7	32.7	85.4	128.8	Proximal right anterior	69.2 ±20.3	0.249	Same as PWS location	-	-
	RAAA	1.31	63.8	37.4	125.6	149.2	Mid-height right dorsal	76.0 ±24.7	0.292	Same as PWS location	Left	Left
2	Asymp-tomatic	-	60.8	48.5	154.7	188.5	Proximal right dorsal	116.6 ±24.0	0.408	Proximal left dorsal	-	-
	RAAA	0.34	69.0	42.2	193.3	156.1	Proximal left	91.0 ±16.2	0.34	Same as PWS location	Left	Left
3	Asymp-tomatic	-	59.0	48.2	241.9	181.7	Proximal left dorsal	91.7 ±24.4	0.403	Same as PWS location	-	-
	RAAA	2.51	84.0	81.4	502.0	288.3	Mid-height right dorsal	146.8 ±49.9	0.801	Same as PWS location	Right	Right
4	Asymp-tomatic	-	43.9	58.2	96.5	176.0	Mid-height left	98.3 ±24.2	0.513	Same as PWS location	-	-
	RAAA	4.73	81.2	131.0	358.7	274.1	Proximal left anterior	151.9 ±38.0	1.441	Mid-height dorsal	Left	Left
5	Asymp-tomatic	-	40.0	59.6	82.1	192.3	Mid-height right dorsal	113.0 ±16.3	0.527	Same as PWS location	-	-
	RAAA	4.85	67.9	85.9	210.5	216.5	Mid-height right dorsal	109.1 ±25.5	0.858	Same as PWS location	Left	Left
6	Asymp-tomatic	-	62.9	92.1	*	229.7	Distal right	127.9 ±32.8	0.949	Mid-height anterior	-	-
	RAAA	0.97	78.8	179.9	303.4	464.7	Distal right dorsal	202.1 ±58.5	2.033	Mid-height left dorsal	Dorsal	Dorsal
7	Asymp-tomatic	-	67.9	102.5	185.8	258.6	Proximal right dorsal	136.1 ±30.0	1.097	Mid-height left dorsal	-	-
	RAAA	0.29	94.2	177.5	271.5	456.2	Distal right	151.7 ±42.1	2.003	Same as PWS location	Left	Left
8	Asymp-tomatic	-	69.1	57.8	284.7	157.5	Proximal left anterior	61.1 ±26.5	0.507	Proximal right dorsal	-	-
	RAAA	1.16	89.9	157.9	477.3	298.2	Mid-height right dorsal	172.0 ±48.8	1.767	Proximal right dorsal	Left	None
9	Asymp-tomatic	-	62.5	64.5	202.7	292.9	Proximal right dorsal	117.8 ±26.9	0.583	Same as PWS location	-	-
	RAAA	2.00	100.6	57.6	*	274.6	Proximal right dorsal	85.2 ±42.3	0.505	Same as PWS location	Right	Left-anterior
10	Asymp-tomatic	-	49.2	45.9	103.1	180.1	Mid-height right dorsal	104.0 ±17.4	0.38	Same as PWS location	-	-
	RAAA	2.48	76.2	68.5	222.3	268.3	Mid-height left	101.2 ±31.9	0.634		Left	None

continued

Table E4. Patient-Specific Geometrical and Biomechanical Results *(continued)*

Patient no.	AAA	Time between scans (years)	Max. external diameter (mm)	RRED (mm)	Total volume (cm^3)	PWS (kPa)	PWS location	Mean WS (kPa)	PWRR	PWRR location	Retroperi-toneal hematoma, predominant location	Visible contrast extra-vasation
										Same as PWS location		
11	Asymp-tomatic	-	68.5	111.0	*	306.3	Mid-height left	131.8 ±31.2	1.201	Same as PWS location	-	-
	RAAA	1.95	111.1	225.9	*	457.0	Mid-height left	152.1 ±50.7	2.587	Same as PWS location	Right	None
12	Asymp-tomatic	-	38.4	38.1	59.1	146.7	Proximal right	82.0 ±12.7	0.301	Same as PWS location	-	-
	RAAA	2.64	55.5	47.0	115.3	188.2	Proximal right	83.7 ±15.4	0.388	Same as PWS location	Right	Right-dorsal
13	Asymp-tomatic	-	67.7	32.6	220.2	118.9	Proximal dorsal	65.0 ±17.8	0.248	Proximal dorsal	-	-
	RAAA	7.41	92.0	30.7	316.3	91.6	Proximal dorsal	47.9 ±15.4	0.231	Mid-height dorsal	Right	None

Note–The time interval between 2 scans ranged from 106 days to 7.4 years. Maximal external AAA diameter increased from pre- to post-rupture state in all patients. PWS, PWRR, and RRED increased in 10 patients from pre- to post-rupture state. RRED was smaller than the actual diameter in 7/13 pre- and post-rupture AAAs.
AAA = abdominal aortic aneurysm; PWRR = peak wall rupture risk; PWS = peak wall stress; RAAA = ruptured abdominal aortic aneurysm; RRED = rupture risk equivalent diameter.
*Volume was not measured.