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Progression of abdominal aortic aneurysm towards rupture - refining clinical risk assessment using a fully coupled fluid-structure interaction method

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Abstract

Rupture of abdominal aortic aneurysm (AAA) is associated with high mortality rates. Risk of rupture is multi-factorial involving AAA geometric configuration, vessel tortuosity, and the presence of intraluminal pathology. Fluid structure interaction (FSI) simulations were conducted in Patient based computed tomography (CT) scans reconstructed geometries in order to monitor aneurysmal disease progression from normal aortas to non-ruptured and contained ruptured AAA (rAAA), and the AAA risk of rupture was assessed. Three groups of 8 subjects each were studied: 8 normal and 16 pathological (8 non-ruptured and 8 ruptured AAA). The AAA anatomical structures segmented included the blood lumen, intraluminal thrombus (ILT), vessel wall, and embedded calcifications. The vessel wall was described with anisotropic material model that was matched to experimental measurements of AAA tissue specimens. A statistical model for estimating the local wall strength distribution was employed to generate a map of a rupture potential index (RPI), representing the ratio between the local stress and local strength distribution.

The FSI simulations followed a clear trend of increasing wall stresses from normal to pathological cases. The maximal stresses were observed in the areas where the ILT was not present, indicating a potential protective effect of the ILT. Statistically significant differences was observed between the peak systolic stress (PSS) and the peak stress at the mean arterial pressure (MAP) between the three groups. For the ruptured aneurysms, where the geometry of intact aneurysm was reconstructed, results of the FSI simulations clearly depicted maximum wall stress at the *a-priori* known location of rupture. The RPI mapping indicated several distinct regions of high RPI coinciding with the actual location of rupture.

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Conflict of Interest

The authors declare that there are no conflicts of interest.

The FSI methodology demonstrates that the aneurysmal disease can be described by numerical simulations, as indicated by a clear trend of increasing aortic wall stresses in the studied groups, (normal aortas, AAAs and ruptured AAAs). Ultimately, the results demonstrate that FSI wall stress mapping and RPI can be used as a tool for predicting the potential rupture of an AAA by predicting the actual rupture location, complementing current clinical practice by offering a predictive diagnostic tool for deciding whether to intervene surgically or spare the patient from an unnecessary risky operation.

Introduction

Rupture of Abdominal Aortic Aneurysms (AAAs) is associated with high mortality rates. Rupture occurs when the mechanical stress exceeds the strength of the vascular tissue. The local wall stress in conjunction with the local wall strength degradation during aneurysmal disease progression is affected by interdependent causes like biomechanical and biochemical processes, AAA geometric configuration, age, family history, and health quality¹⁻⁴. Of a special interest to the clinical practice is an effective patient specific rupture risk assessment, which is currently based on the less refined and at times inaccurate AAA diameter and growth rate criteria.

A variety of ways have been proposed to a modeling approach for patient specific rupture risk assessment, generating a tradeoff between accuracy and degree of complexity of the simulation methods which necessarily translates into computational processing time. AAA classification based on a combination of geometrical features derived from non-invasive clinical imaging appears attractive since a great percentage of the computational time and cost is avoided.^{5, 6} A challenging aspect of such approach is deciding which AAA geometric configurations clearly pose a risk of rupture before handing such an important tool to the clinicians, i.e., identifying those AAA geometrical parameters that have the potential to provide a safe marker of the rupture risk threshold. Data mining which facilitates the identification of patterns within data sets was used to correlate geometrical parameters with the AAA repair status concluding that sac length, sac height, volume, surface area, maximum diameter, bulge height and ILT volume can offer useful information⁷. Image based detection of the lumen centerline was also considered for AAA classification prior to rupture risk estimations⁸. Surface curvature was also analyzed as a classifier-proven to yield more accuracy in the risk prediction than diameter⁹.

The most accurate practice to indicate the risk threshold though is the quantitative mapping of patient-specific wall stress and strength. Due to the inherent limitations of measuring directly or estimating indirectly the wall stresses or tissue strength of AAAs *in-vivo*, computational models offer a robust option. Mapping and quantifying the stresses developing within the aneurysmal wall of patient specific AAAs can help clinicians determine the need for surgical intervention. Previous studies based on less accurate and non-dynamic AAA simulations have shown that computational models can be 12% more accurate and 13% more sensitive than using maximum diameter as sole rupture risk predictor (e.g., Fillinger et al.^{10, 11, 12}).

Wall stresses have been calculated mostly by structural analysis of the aneurysm sac employing static uniform pressure acting on the intraluminal surface¹³. This approach does not take into account the spatiotemporal dynamic pressure distribution due to the luminal hemodynamics¹⁴. Besides AAA luminal hemodynamics, a proper model for accurate prediction of stresses developing within the AAA wall requires patient specific AAA geometries, information about inlet velocity components and dynamic pressure distribution^{4, 15, 16}. Estimation of individual constitutive material models that describe the mechanical response of AAA tissue and the local wall thickness¹⁷ and its variability¹⁸⁻²⁰ further augments the fidelity of the numerical simulation and its predictive capabilities. The importance of the regional variations in material anisotropy, stiffness and wall thickness are highlighted in²¹⁻²⁵ to reiterate the need of more reliable modelling techniques and better understanding the mechanobiology of the lesion¹.

There are inherent modeling challenges regarding characterizing the biomechanical behavior of the AAA ILT²⁶ (elastic, hyperelastic, poroelastic, porous) and calcifications²⁷, increasing significantly the complexity of the problem. Di Martino et al. have shown that the presence of ILT can significantly reduce wall stresses²⁸⁻³⁰. The resulting magnitude and location of the peak wall stresses was dependent on the shape of the AAA. Complex flow trajectories within the AAA lumen indicated also a putative mechanism for the formation and growth of the intraluminal thrombus (ILT). Our previous studies^{31, 32} suggest that thrombus reduces stresses on the aneurysmal wall without significantly changing location of maximum stress.

FSI simulations, in which a fully coupled dynamic interaction between the AAA hemodynamics and wall deformations is modeled, were conducted by our group^{31, 32} and others to simulate the biomechanical behavior of the AAA wall^{10, 29, 33-40}. Most previous FSI studies were based on isotropic material models that exclude the directional response of abdominal aortic tissue to stresses. Our group performed FSI studies in patient specific geometries reconstructed from CT scans in AAAs of varying configurations, both with and without intraluminal thrombus^{32, 34}. Experimental data of biaxial stress measurements⁴¹ was fitted to an orthotropic material model which simulates vessel tissue as fiber-reinforced composite material⁴²⁻⁴⁶. Computational modeling is gaining ground as a risk predictor but needs further validation before getting utilized in a large scale from clinical perspective. To this end, experimental settings have also emerged to indicate either convergence or divergence of the computational results⁴⁷.

In our previous work we have verified that the FSI methodology we have developed was able to predict the actual rupture location of AAA on a patient specific basis³¹. We have further compared the rAAA stress results with cases of normal aortas and cases of AAAs that did not rupture. In this study we expand the cohort of normal and pathological cases to describe hemodynamic and wall structural changes differentiating AAAs during disease progression by studying the aforementioned three groups, (normal aortas, non-ruptures AAA and ruptured AAAs). The analysis, based on maximum von Mises stress (isotropic material model) and maximum principal axis stress (orthotropic material model), at peak systole and at MAP, combined with statistical test for the three groups provide a trend (nomogram) and adaptation response of the abdominal aorta behavior during these three stages of the disease.

We further discuss the potential contribution of important biomechanical features of AAA such as the role of ILT and calcifications on the pathological aortic wall.

Methods

Using patient specific FSI methodology we characterize in this study AAA disease by studying three distinct stages of the disease succession, from normal aortas to non-ruptured AAA and to ruptured AAAs.

Acquisition of CT data

Abdominal Computed tomography (CT) scans were acquired with intravenous contrast, which is the standard of care for AAA disease patients, from patients who arrived at the Stony Brook university hospital ER or at the Liege University Hospital, Belgium, with contained ruptured AAA, aneurysmal non-ruptured aortas, retrospectively (i.e., fissure type of rupture, where the AAA geometry did not drastically change because of the rupture and there was enough time to scan the patient before the surgery. Accordingly the ruptured AAA (rAAA) shape remained intact). CT scans of normal aortas were also obtained and used as baseline control cases. Informed consent was obtained retrospectively for all cases. The protocol was approved by the Institutional Review Boards (IRB) Committees on Research Involving Human Subjects of the corresponding institutions. Overall, twenty-four aortic CT scans with intravenous contrast were acquired, eight normal aortas and sixteen pathological aortas, (8 aneurysmal non-ruptured aortas and 8 contained ruptured AAA).

Patient specific approach for Fluid-Structure Interaction

The coordinate points and dimensions of patient specific AAA geometry were extracted from the CT scans, including anatomical details of the vessel wall, lumen, ILT, and calcifications (Ca). For the normal and pathological abdominal aortas, boundaries of the reconstructions were established from just below the renal arteries branching until 4.0 cm distal to the iliac bifurcation. Other smaller arteries, such as the gonadal and lumbar/spinal arteries, the inferior mesenteric artery and the median sacral artery were neglected due to lack of information about the blood flow exiting these arteries and their marginal effect on AAA hemodynamics. A uniform thickness of 2mm was assigned to the AAA wall, as used in previous studies of patient specific geometries^{36, 41, 48, 49}. The parallel planes scans were translated into 3D images using Mimics (Mimics, Materialise, Leuven, Belgium) and MMS (MMS, Medical Metrx Solutions Inc., West Lebanon, NH). The twenty-four aortic geometries were reconstructed in detail with the use of advanced image reconstruction software packages.

The obtained 3D geometries were further discretized into triangular elements meshes for fluid structure interaction (FSI) simulations (ADINA R&D, Inc., Watertown, MA). Figures 1a and 1b show the coronal and axial views of the CT data overlaid by the reconstructed 3D geometry. Figure 1c shows the 3D reconstruction of one of the eight contained ruptured aneurysm (rAAA) elected for studying with the patient-based FSI methodology.

Material properties of the aortic wall

Isotropic and orthotropic material model formulations have been used in this study. The orthotropic material formulation models the arterial wall as a composite deformable structure that exhibits non-linear stress-strain relationship with exponential stiffening at high stresses⁵⁰⁻⁵². A typical value of the angle between the two families of fibers characterizing AAA wall biomechanics was extracted from the literature³². In this study we employ higher order terms in the isotropic Mooney-Rivlin (M-R) strain energy function⁵³ to account for the departure from neo-Hookean/Gaussian behavior at large stretches, combined with the Holzapfel orthotropic^{50, 54} material formulations.

The isochoric elastic response for our isotropic material model formulation, $\bar{\Psi}_{iso}$, is given in eq. (1).

$$\bar{\Psi}_{iso} = C_1 (I_1 - 3) + C_2 (I_1 - 3)^2 + D_1 \left(e^{D_2(I_1-3)} - 1 \right), \quad I_1 = \text{tr}(C_{ij}). \quad (1)$$

Where I_1 , is the first invariant of the Cauchy-Green deformation tensor. The isochoric elastic response for the orthotropic material model formulation, $\bar{\Psi}_{aniso}$, is given in eq. (2).

$$\bar{\Psi}_{aniso} = \bar{\Psi}_{iso} + \frac{k_1}{2k_2} \sum_{i=4,6} \left[e^{k_2(J_i-1)^2} - 1 \right], \quad (2)$$

$$J_4 = J^{-1/3} I_4, \quad I_4 = C_{ij}(n_a)_i(n_a)_j, \quad J_6 = J^{-1/3} I_6, \quad I_6 = C_{ij}(n_b)_i(n_b)_j, \quad J = \det(C_{ij}).$$

Where J , is the third invariant of the Cauchy-Green tensor C_{ij} , n_a and n_b are the directions of the fibers defined by two angles, a_a and a_b , which are offset from the material axes⁵⁴. A displacement-pressure finite element formulation was used where the pressure is not a part of the potential function and is separately interpolated⁵⁵. More details of the model used in our FSI simulations can be found in elsewhere^{31, 32}.

The combined strain energy formulation used in our FSI simulations³² produced excellent fit to previously published biaxial stretching experimental data with AAA specimen⁴¹. The parameters that best fit the model are shown in Table 1 ($R^2 = 0.99$). This r-square value is very high and it could be due to a small bias in our initial fit. Using the above orthotropic model, a replication of this bi-axial tensile testing⁴¹ was conducted numerically in order to validate the model parameters. Briefly, a square 2 cm specimen was recreated in ADINA software package, and the stress-strain relationship in the circumferential and longitudinal directions was matched against the experimental results. Loading on each edge started at 0 N/m, then incrementally increased to 120 N/m over 1 s. The stress-strain relationship in both directions was averaged at four elements at the corners of a $5 \times 5 \text{ mm}^2$ square near the center of the plate. A good agreement was achieved between the stress-strain relationship of the simulated specimen and the experimental measurements³².

The ILT material was modeled as linear elastic with a Young's modulus of 0.11 MPa and a Poisson ratio of 0.45^{36, 56}. Small calcifications (small-Ca) were assumed to behave as a stiff isotropic material with properties summarized in Table 1^{57, 58}. In the results presented we calculate the von Mises stresses for the isotropic material models and the principal p_1 stresses for the orthotropic material model. These stresses provide a quantitative value of the

wall stress at each point on the external wall surface, presented as a three-dimensional color mapping corresponding to the stress level.

FSI methodology

The fluid domain is governed by the Navier-Stokes and the continuity equations. The Arbitrary Lagrangian Eulerian moving mesh approach is utilized for re-meshing the fluid domain at each time step. We apply a fully coupled implicit-dynamics FSI approach with a sparse solution process. The numerical simulations utilize direct coupling between the blood, and the solid, vessel wall⁵⁹. A finite-element scheme is used to solve the set of motion and fluid equations using the ADINA software package (ADINA R&D, Inc., Watertown, MA).

For the fluid domain, time dependent flow and pressure conditions measured by Olufsen et al.⁶⁰ are prescribed as boundary conditions at the outlet and inlet of the AAA geometry. More details about the waveforms can be found elsewhere³¹. Blood is modeled as a homogenous Newtonian fluid, with a density of 1035kg/m³ and a viscosity of 3.5cP³² and the flow was considered laminar. All models are assumed to be initially at zero stress state, with the residual stress field in the unloaded configurations not considered. An initial stress loading is achieved by pressurizing the AAA from 0 mmHg to 90 mmHg with zero flow for one second, before the FSI waveforms are applied. For the solid domain, all degrees of freedom are fixed at the inlet and outlets. Each computation was continued for four complete flow cycles using a time step of 4×10^{-3} s. The Newton iteration scheme was used for the sparse matrix solver, with 0.001 relative tolerance for all the degrees of freedom^{31, 32}.

In the fluid domain, four node tetrahedral flow based control interpolation (FBCI) elements were used. Four node tetrahedral elements were used for the wall and ILT. In all simulations that contained an ILT, faces that were shared between the outer wall and the ILT were linked so that nodes generated on the face are used for both the ILT and the wall. Mesh convergence studies in which flow parameters and stress/displacement analyses with coarser and finer meshes were tested, established that the results are mesh independent³².

Wall strength and Rupture Potential Index (RPI)

A statistical model of non-invasive means to calculate *in vivo* wall strength distribution was employed⁶¹. It lumps together significant clinical and geometric predictors to yield a local value of the wall strength such as the local attached ILT thickness in cm, the local diameter normalized to the diameter of non-aneurysmal aorta (infrarenal) estimated from the patient's age and sex⁶², the family history (½ with history, -½ without history) and patient's gender (½ male, - ½ female)⁶¹. This model is used to generate 3D mapping of the wall strength that is then compared to the local stress distribution, to generate a map of a rupture potential index (RPI), defined as the ratio between the locally acting wall stress (calculated by FSI) and the local wall strength. Each global predictor variable, e.g., family history and AAA size, were obtained from each patient's hospital chart, while spatially varying predictor variables, local diameter and ILT thickness, were measured from CT images.

Statistical Methods

The obtained data were expressed by their mean and standard deviation (mean $\pm$ SD) values. Non-parametric one-way variance analysis (ANOVA) was utilized for examining significance of stress levels at peak systole or at mean arterial pressure, $MAP = p_d + 0.33(p_s - p_d)$, where p_s and p_d denote systolic and diastolic pressures, for the three groups (normals, AAA and rAAA). This test was performed to discern statistical differences among maximum von Mises stress values from our FSI simulations. Since the maximum stress values used in statistical analysis represent independent experimental end points, $p < 0.01$ was considered to determine statistical significance. Statistical analysis was performed using in house Matlab script (MathWorks, Natick, Massachusetts, USA).

Results

Blood flow through aneurysmal and normal aortas

The FSI approach can provide a detailed representation of the flow field during the cardiac cycle for the normal and the pathological aortic lumens. For all aneurysmal cases the flow patterns during peak systole change significantly as compared to healthy aortas. The abrupt expansion from the aneurysm neck to the dilated AAA lumen induces a rapid decrease in the velocities followed by the formation of complex flow patterns and recirculation zones^{31, 63}. Figure 2a shows the flow field in the aneurysmal sac for six representative cases 0.15 s after the peak systole. It is observed that while the flow field is streamlined at the two normal aortas, the flow becomes clearly disturbed for the two non-ruptured AAAs. The disturbances are intensified for the last two pathological ruptured cases (rAAAs) where the formation of recirculation zones is clearly depicted. During diastole, large and diffuse, recirculation zones are formed in both AAAs and rAAAs models. These are more pronounced as the aneurysmal sac widens and span almost the entire diameter of the aneurysmal bulge. In both pathological cases, smaller recirculation zones can be observed to form in the flow field, occurring either at the inlet of the aneurysm or close to the stagnation area of the iliac bifurcation during diastole, producing highly complex disturbed flow patterns.

The changes in the velocity field and in the flow patterns result in significant changes in the luminal pressure distribution as compared to the normal aortas. At peak systole, the typical blood pressure acting on the wall at the normal aortas 1cm above the iliacs was approximately 120mmHg, whereas in the pathological cases (rAAAs group) it was, 2% - 3% higher (122.4mmHg - 123.6mmHg). The blood pressure during diastole was also higher in the pathological cases (rAAAs group) as compared to the normal cases. For instance, at 60% of the cardiac cycle (early diastole), the pressure in the normal aorta 1cm above the iliacs was 104.5 mmHg whereas the pressure at the same location was 0.4% - 0.6% higher for the rAAAs remaining almost constant throughout the aneurysm and dropped abruptly at the iliac arteries. This indicates that, in AAAs, there is an increase in the pressure acting on the aortic wall, which is not compensated by the expected downstream pressure drop.

Wall stress distribution in the aortic wall

Results during peak systole and at mean arterial pressure (MAP) with isotropic and anisotropic wall formulations are presented in Table 2, with von Mises stresses reported for

the isotropic simulations and principal axis (p_1) wall stresses reported for the anisotropic simulations, correspondingly (see Appendix for additional information on the FSI simulation). Figure 2b shows the peak von Mises stresses for six representative cases. There is a general trend of rising wall stresses from normal aortas to non-ruptured and ruptured AAAs as depicted in Figure 3a. In this figure the maximum peak systolic von Mises stress is plotted against the maximum diameter of the aorta for each case. Progressing to the pathological cases, from normal subjects to non-ruptured AAA and then to rAAA, the maximum diameter increased and the maximum stress was also increased, following a non-linear curve.

Normal subject models have a mean value of peak maximum von Mises stress of 0.37 MPa with standard deviation ± 0.057 MPa. Isotropic simulations for non-ruptured aortas reach a mean peak systolic von Mises stress of 0.62 MPa with standard deviation ± 0.3 MPa. Ruptured AAA cases produce much higher wall stresses, with mean peak systolic von Mises stresses reaching 1.23 MPa with standard deviation ± 0.51 MPa, Table 2. Similarly, normal subject models have a mean MAP von Mises stress of 0.29 MPa with standard deviation ± 0.043 MPa. Isotropic simulations for non-ruptured aortas reach a mean MAP von-Mises stress of 0.44 MPa with standard deviation ± 0.22 MPa. Ruptured AAA cases produce higher wall stresses, with mean MAP von Mises stresses of 0.91 MPa with standard deviation ± 0.47 MPa, Table 2.

The FSI anisotropic material simulations follow the same trend as the isotropic simulations. Principal axis stress, p_1 , significantly increasing from normal to pathological cases as shown in Table 2. All anisotropic simulations showed higher peak wall stresses as compared to the isotropic material model formulation. For the rAAA cases the percentage difference between isotropic and orthotropic material models was 3.3% (rAAA5) and 25% (rAAA8) for the two reported cases. Both von Mises distribution for the isotropic material formulation and principal axis stresses distribution for the anisotropic material formulation became highly non-uniform as the vessel wall progressed from a normal to an aneurysmal pathology³¹.

The FSI simulations performed in all patients with ruptured AAA indicated highest stresses along and around the actual rupture line, with a good agreement as shown in Figure 4. In this figure the stress concentrations of four representative contained rAAAs (one from each diameter group studied) are presented (see also Figure 1Ap of the Appendix for all ruptured AAAs). The arrows in Figure 4 indicate the actual rupture location (known a priori from ER CT scans). The result was also confirmed in our previous study³¹. More details about these structures, e.g. maximum peak systolic wall stress, maximum peak wall stress at MAP, maximum diameter etc, are shown in Table 2 and in Appendix.

Role of calcifications in AAA

In order to study the effect of calcifications in AAAs we divided the calcified spots into two broad categories. The first type of calcifications is defined as small calcified spots (small-Ca) – such as those appearing near the location of rupture, with a maximum diameter smaller than 4.0 mm. The second type is the large plaque-like calcified spots. FSI simulations were performed for some cases of the non-ruptured and ruptured AAA with and without the presence of small or plaque-like Ca for comparison purposes. In the non-

ruptured AAA, small-Ca embedded in the wall, distal to the ILT location, increased the local stress within the wall by up to 36.8% as compared to the FSI simulation without the small-Ca for the anisotropic material wall model formulation. Additional FSI simulation performed for a larger, plaque-like Ca, reconstructed from CT data for a rAAA, indicated a reduction of the local wall stresses near the calcification by 21% as compared to the FSI simulation without the plaque-like Ca (for both material model formulations). More details about the results for the effect of calcified spots in rAAAs at the location of rupture can be found elsewhere³¹.

Rupture Potential Index

The resulting rupture potential index (RPI - the ratio between the locally acting wall stress from the FSI simulations and the local wall strength) for four representative pathological cases (two non-ruptured AAA and two rAAA) are shown in Figure 2c. The rupture potential index (RPI) calculations are based on stress distribution derived from FSI simulations without the effect of the calcifications. The mapping of the RPI indicated several distinct regions of high RPI, with at least one coinciding with the actual location of rupture for the rAAA cases. The maximum RPI for all rAAA cases is close or higher to unity, ranging from 0.8 to 1.339, with a mean value of $\text{RPI } 0.965 \pm 0.22$, indicating a very high risk of rupture for all 8 rAAAs (Table 2). The maximum RPI for the non-ruptured AAA has smaller values, ranging from 0.39 to 0.693, with a mean value of $\text{RPI } 0.54 \pm 0.115$, indicating a milder risk of rupture for the non-rupture AAA (Table 2).

Similar to the general trend of rising wall stresses from normal aortas to non-ruptured and ruptured AAAs is the trend for the RPI, as depicted in Figure 3b. In this figure the maximum RPI is plotted against the maximum diameter of the pathological aortas (AAA and rAAA). Moving from non-ruptured AAA to ruptured AAA, the maximum pathological diameter increases and the maximum RPI is also increased, following a non-linear curve.

Statistical analysis of peak wall stress at peak systole and at mean arterial pressure (MAP) for the three groups

Non-parametric one-way variance analysis (ANOVA) was utilized for examining significance of stress levels at peak systole or at mean arterial pressure, MAP, for the three groups (normals, AAA and rAAA). Figure 5 shows the Box and Whisker plots for peak stress at peak systole and mean arterial pressure (MAP) for the three different groups. The test showed statistical differences among the three groups at peak systole and MAP, with $p = 0.001$ and $p = 0.0004$, respectively.

Discussion

An advanced methodology of patient specific fluid-structure interaction (FSI) approach using orthotropic material models characterizing the biomechanical response of the aortic wall is presented, for better estimation of the risk of rupture in AAAs. The methodology is based on patient-specific reconstructed geometries and a careful biomechanical characterization of the aortic wall behavior based on experimental data⁴¹. Following our previous studies, in this study we expand the cohort of normal and pathological cases to

describe the hemodynamic and structural progression of the AAA disease by studying three groups, (normal aortas, non-ruptures AAA and ruptured AAAs). Differences between normal aortas and abdominal aortic aneurysms (statistically analyzed) were studied.

Eight cases of contained ruptured aneurysms were specifically studied in order to test the ability of the methodology to predict the actual rupture location. Specifically, Figure 4 shows the stress concentrations of four representative contained rAAAs (one from each diameter group studied – all cases are presented in the Appendix). The arrows indicating the actual rupture location (known a priori from the ER CT scans) closely overlap the regions corresponding to the highest wall stress mapped, with apparent stress concentrations in these regions. Although there are larger regions that may appear with high stresses, these smaller localized regions of stress concentrations characterized by the peak stress values found in the specific rAAA, appear to be those indicating an AAA prone to rupture. Apparently they serve as better predictors for the AAA risk of rupture. These stress concentrations appear to occur in regions of sudden geometric changes (e.g., from the ascending aorta into the aneurismal sack, between the AAA and the iliac bifurcation, etc.), and in most of the cases have other contributing factors such as small-Ca embedded in the aortic wall in these regions, which are known to generate localized stress concentrations. Clearly surgeons should be more aware of the importance of such AAA characteristics when diagnosing a specific patient's AAA risk of rupture, with more attention given to these factors over the size of the aneurysm. Additional details about these structures, e.g. maximum peak systolic wall stress (von Mises stress), maximum peak wall stress (von Mises stress) at MAP, maximum diameter etc, are shown in Table 2 and in the Appendix. More details about rAAA5 and rAAA8 can be found elsewhere³¹. Isotropic and anisotropic material model formulations were used to characterize the biomechanical response of the aortic wall, and FSI simulations were performed using physiological blood flow conditions. The analysis based on peak wall stress (at peak systole and at MAP) combined with a statistical test for the three groups provide a trend (nomogram) of the aortic behavior during the three stages of the disease.

Blood flow in aneurysmal aortas exhibit complex dynamic flow patterns that completely deviate from those of the normal aortas, highlighting the importance of analyzing the AAA hemodynamics and their interaction with the aortic wall when studying AAA risk of rupture. The peak velocities during systole are lower in pathological aortas as compared to normal aortas, a clear result of large and secondary smaller recirculation zones characterizing AAA flow fields, mostly during the diastolic phase, that in turn alter the pressure and the wall shear stress (WSS) distributions during the cardiac cycle³¹. In all FSI simulations the pressure field of the pathological aortas increased during the cardiac cycle, as compared to the normal cases. This clearly indicates that in AAAs there is an increase in the pressure acting on the aortic wall, which is not compensated by the expected downstream pressure drop. This effect is inherently ignored by a modeling approach that utilizes structural analysis only, applying static pressure. It may be hypothesized that this pathological dynamic pressure increase (2% - 3% during the systolic phase) could be the driving force for the abnormal aortic expansion during the aneurysm expansion, in combination with additional biomechanical factors.

Simulations with isotropic and anisotropic material model formulations indicated a consistent pattern of increasing peak wall stresses from normal aortas to non-ruptured and ruptured AAAs. This trend of increasing wall stresses demonstrates the capability of the methodology to characterize biomechanical determinants in different stages of the aortic wall (normal aorta, non-ruptured AAA, ruptured AAA). The values of wall stresses predicted by our models are in agreement with previously published ruptured and non-ruptured AAA studies, performed by our group^{31, 32} and other researchers^{2, 13, 14, 47}. The FSI simulations with reconstructed rAAA demonstrate that the location of the maximal wall stresses overlaps the actual rupture region. These results suggest that our methodology can predict the potential location of the rupture by depicting and quantifying regions of high wall stresses.

Special attention was given to the orthotropic material model development. The orthotropic material formulation models the arterial wall as a composite deformable structure that exhibits nonlinear stress–strain relationship with exponential stiffening at high stresses. This stiffening effect results from simulating an embedded mesh of two families of collagen fibers which lead to the characteristic anisotropic mechanical behavior of arteries³¹. Many studies have identified the important role of the aortic wall material anisotropy as well as the stiffening and thickening process of the aortic wall due to aging and pathology²¹⁻²⁵. Recent literature suggests that the wall morphology is still not well described or understood and additional research is required. Ferruzzi et al. claim that a structurally motivated phenomenological four fibers family constitutive relation captures the biaxial mechanical behavior of both human AAs (ages less than 30 to over 60) and AAAs, much better than existing material models⁶⁴. They suggest that their model captures the loss of structural integrity of elastic fibers due to ageing and the development of abdominal aneurysms, thus improving the ability to predict disease progression. Gasser et al., further developing their previous model which was used in this study, indicate that the undulation of collagen fibers in the unstressed tissue is a structural parameter with significant mechanical impact that needs to be further investigated⁶⁵. They introduce new constitutive models for collagen fibers that integrate the structural information in a macroscopic AAA wall model.

Accurate prediction of the AAA risk of rupture entails the ability to predict whether the wall will actually fail. This requires weighing the local wall stress against the local wall strength. The latter involves information that can be indirectly estimated by factoring in biomechanical and clinical parameters, as well as the medical history of the specific patient. The RPI⁶¹ that was incorporated in our methodology to achieve such an estimate. The RPI mapping depicted distinct locations more prone to rupture (Figure 2c). The strength and RPI calculations were performed without Ca for all cases studied.

There is a debate in the recent literature whether the presence of ILT plays a protective role on the aortic wall. Di Martino et al. have shown that the presence of ILT can significantly reduce wall stresses²⁸⁻³⁰. In this study, our simulations reveal that the ILT plays a cushioning role with reduced stresses on its vicinity. This result is based exclusively on a mechanical point of view and not at any biochemical effect such as wall degradation that the ILT could cause on the aortic wall. However, there are studies that discuss the opposite

effect, which is that the ILT is associated with higher growth rate leading eventually to a gradual weakening of the AAA wall^{66, 67}.

Our study indicates that an approach that is quantitatively based on stress and RPI distributions and takes under consideration the coupling of the arterial wall with the hemodynamic properties may offer a refined alternative to the current decision for AAA treatment. It is clear that at least a moderate number of comparative cases for small and large-size AAA patient group is needed to further establish the clinical validity of this approach. In this study we substantially expand the cohort of normal and pathological cases compared to our previous studies³¹. This expansion provides statistical significance between the three studied groups and establishes the validity of the FSI approach. The patient-based FSI methodology developed can clearly distinguish the three different studied groups (normal aortas, non-ruptured AAA and rAAA), as shown in Figure 3, and also provides a nomogram of the aortic behavior during the three stages of the disease.

There are currently different thresholds for intervention accepted in the United States (5cm) compared to Europe (5.5 cm). Maximal aneurysm diameter is a crude predictor of rupture risk, since some smaller aneurysms do rupture and some larger ones remain intact. To avoid unfortunate situations which may either put patients at unnecessary intervention risk or underestimate their risk of rupture, current decision models clearly require more detail and more specificity. Refinement of our ability to predict AAA rupture risk is vital for providing appropriate therapies to the maximal number of patients. It is clear that biomechanical considerations can both improve our understanding of aneurysmal disease progression and refine our ability to predict the risk of rupture.

Limitations

While we introduce a refined approach based on the pertaining biomechanical considerations such as geometry of the aneurysm and the interaction with the hemodynamic properties, a patient-specific modeling aimed at AAA diagnostics could always benefit from incorporating additional patient-specific data beyond these offered by the current study. Similar to other recent studies that used routinely acquired CT scans of AAA patients, the results presented are based on the assumption of a uniform 2 mm wall thickness, which may distort the stress values and their distribution. Models that use additional clinical modalities that describe in details the local wall thickness¹⁷ and its variability¹⁸⁻²⁰ could further augment the fidelity of the numerical simulation and improve their predictive capabilities. In the current study this assumption was necessary due to limitations in the imaging and reconstruction techniques, but bears minimal effect on the comparison between the two material models and the effects of the ILT as previously demonstrated by our group³². However, our study goes a step beyond current advanced current modeling efforts that mostly incorporate isotropic hyperelastic material models, or anisotropic material models but employ static simulations. This is a demonstration of the ability of FSI simulations employing more accurate characterization of the aneurysmal wall biomechanical properties, to predict the location of potential rupture and to compare it to its local strength.

While the methodology demonstrates the ability to distinguish the alterations between different stages of the disease (normal aortas, non-ruptured AAA and ruptured AAA), in this

specific study we have compared normal and pathological aortas of different patients in a retrospective study. In future studies we plan to conduct longitudinal studies in which AAA progression will be monitored and analyzed in the same patients during the disease progression (prospective study). In these future studies intermediate results from the FSI calculations could be experimentally verified. Those include flow field development, fluid pressure and wall shear stress. Another limitation of the reconstructed rAAA geometries is possible reconstruction implications of the ruptured aortas. In that aspect we carefully chose only contained ruptured aneurysms (fissure type of rupture) so that the geometry did not significantly change because of the rupture and till the patient was operated. Additionally, abnormal local curvature of the aneurysmal geometry could play a role on the stress distribution and local structure “singularities” could lead to localized stress hot spots. However, the reconstructed rAAA structures were smoothed and the final computational grids were without points of “sharpness”. The performed grid independence studies at the initial rAAA structures provide also confidence about our results and eliminate issues concerning anomalies due to the computational mesh.

The residual stress field in the unloaded configurations was not considered due to the complexities involved, which could lead to a less uniform transmural stress field in the simulated configurations. However, this simplification was partially rectified by pressurizing the AAA geometric configurations from an initial zero stress condition to 90 mmHg with zero flow for 1 s, before the FSI waveforms were applied. At this loading stage and for all AAA structures we did not notice a discernible change in the shape of the preloaded configuration as compared to the unloaded reconstructed geometries.

The most consistent approach for studying aneurismal disease progression would be to include also the patient specific hemodynamic characteristics (actual flow rate and pressure waveforms measured at the time of the CT scan). However, this study in such a large cohort of patients was retrospective and this information was not available. In our initial work we did not account for peripheral resistance, rather we applied dynamic pressure waveforms. Since this work is a continuation of our previous studies and in order to provide the same conditions for comparing all cases studied, we applied uniform boundary conditions in all cases. The value of applying uniform boundary conditions across the board for all patients is in conducting a controlled comparative study. This was one of the goals of this large cohort study - namely, comparing the biomechanical response during the aneurismal disease progression. In future studies we plan to incorporate in the FSI simulations peripheral resistance by incorporating in the models compartmental models⁶⁸. Nevertheless, the inlet velocity boundary condition used in this study leads to physiological flow rates for all cases (normal and pathological aortas).

The current work shows that even when employing many simplifying assumptions, a methodology that is based on pure biomechanical considerations demonstrates a powerful predictive capability that could vastly improve the diagnostics of patients with AAA disease. The methodology challenges current clinical practice, where a risky elective repair of the AAA based on its size alone is warranted rather than looking at a patient-specific stresses developing within the aneurysmal wall as a result of the complex interaction between the AAA geometry, hemodynamics, and the wall mechanical response. The FSI approach shows

an increasing trend with stresses significantly increasing from normal to pathological cases. The results demonstrate that FSI wall stress mapping and RPI can be used as a tool for complementing the current clinical practice. The proposed methodology may provide clinicians and surgeons with a refined diagnostic and decision tool for establishing the need for a risky surgical intervention, by providing a fully dynamic and quantitative depiction of the AAA biomechanics under hemodynamic conditions, and predicting its risk of rupture.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

References

1. Humphrey JD, Holzapfel GA. Mechanics, mechanobiology, and modeling of human abdominal aorta and aneurysms. *Journal of Biomechanics*. 2012; 45:805–814. [PubMed: 22189249]
2. McGloughlin TM, Doyle BJ. New approaches to abdominal aortic aneurysm rupture risk assessment engineering insights with clinical gain. *Arterioscler. Thromb. Vasc. Biol.* 2010; 30:1687–1694. [PubMed: 20508202]
3. Michel JB, Martin-Ventura JL, Egido J, Sakalihasan N, Treska V, Lindholt J, Allaire E, Thorsteinsdottir U, Cockerill G, Swedenborg J, Consortium FE. Novel aspects of the pathogenesis of aneurysms of the abdominal aorta in humans. *Cardiovasc. Res.* 2011; 90:18–27. [PubMed: 21037321]
4. Raut SS, Chandra S, Shum J, Finol EA. The role of geometric and biomechanical factors in abdominal aortic aneurysm rupture risk assessment. *Annals of Biomedical Engineering*. 2013; 41:1459–1477. [PubMed: 23508633]
5. Washington CB, Shum J, Muluk SC, Finol EA. The association of wall mechanics and morphology: A case study of abdominal aortic aneurysm growth. *Journal of Biomechanical Engineering-Transactions of the Asme*. 2011; 133:6.
6. Doyle BJ, Hoskins PR, McGloughlin TM. Computational rupture prediction of aas: What needs to be done next? *Journal of Endovascular Therapy*. 2011; 18:226–229. [PubMed: 21521063]
7. Shum J, Martufi G, Di Martino E, Washington CB, Grisafi J, Muluk SC, Finol EA. Quantitative assessment of abdominal aortic aneurysm geometry. *Annals of Biomedical Engineering*. 2011; 39:277–286. [PubMed: 20890661]
8. Zhang H, Kheifets VO, Finol EA. Robust infrarenal aortic aneurysm lumen centerline detection for rupture status classification. *Med. Eng. Phys.* 2013; 35:1358–1367. [PubMed: 23608300]
9. Lee K, Zhu JJ, Shum J, Zhang YJ, Muluk SC, Chandra A, Eskandari MK, Finol EA. Surface curvature as a classifier of abdominal aortic aneurysms: A comparative analysis. *Annals of Biomedical Engineering*. 2013; 41:562–576. [PubMed: 23180028]
10. Fillinger MF, Marra SP, Raghavan ML, Kennedy FE. Prediction of rupture risk in abdominal aortic aneurysm during observation: Wall stress versus diameter. *J Vasc Surg*. 2003; 37:724–732. [PubMed: 12663969]
11. Truijers M, Pol JA, Schultzekool LJ, van Sterkenburg SM, Fillinger MF, Blankensteijn JD. Wall stress analysis in small asymptomatic, symptomatic and ruptured abdominal aortic aneurysms. *Eur J Vasc Endovasc Surg*. 2007; 33:401–407. [PubMed: 17137809]
12. Fillinger M. The long-term relationship of wall stress to the natural history of abdominal aortic aneurysms (finite element analysis and other methods). *Ann N Y Acad Sci*. 2006; 1085:22–28. [PubMed: 17182919]
13. Maier A, Gee MW, Reeps C, Pongratz J, Eckstein HH, Wall WA. A comparison of diameter, wall stress, and rupture potential index for abdominal aortic aneurysm rupture risk prediction. *Annals of Biomedical Engineering*. 2010; 38:3124–3134. [PubMed: 20480238]

14. Gasser TC, Auer M, Labruto F, Swedenborg J, Roy J. Biomechanical rupture risk assessment of abdominal aortic aneurysms: Model complexity versus predictability of finite element simulations. *European Journal of Vascular and Endovascular Surgery*. 2010; 40:176–185. [PubMed: 20447844]
15. Chandra S, Raut SS, Jana A, Biederman RW, Doyle M, Muluk SC, Finol EA. Fluid-structure interaction modeling of abdominal aortic aneurysms: The impact of patient-specific inflow conditions and fluid/solid coupling. *Journal of Biomechanical Engineering*. 2013; 135:081001–081001.
16. Erdemira A, Guess TM, Halloran J, Tadepalli SC, Morrison TM. Considerations for reporting finite element analysis studies in biomechanics. *Journal of Biomechanics*. 2012; 45:625–633. [PubMed: 22236526]
17. Shum J, DiMartino ES, Goldhammer A, Goldman DH, Acker LC, Patel G, Ng JH, Martufi G, Finol EA. Semiautomatic vessel wall detection and quantification of wall thickness in computed tomography images of human abdominal aortic aneurysms. *Med. Phys.* 2010; 37:638–648. [PubMed: 20229873]
18. Raut SS, Jana A, De Oliveira V, Muluk SC, Finol EA. The importance of patient-specific regionally varying wall thickness in abdominal aortic aneurysm biomechanics. *Journal of Biomechanical Engineering-Transactions of the Asme*. 2013; 135:10.
19. Tierney AP, Callanan A, McGloughlin TM. Use of regional mechanical properties of abdominal aortic aneurysms to advance finite element modeling of rupture risk. *Journal of Endovascular Therapy*. 2012; 19:100–114. [PubMed: 22313210]
20. Doyle BJ, Callanan A, Grace PA, Kavanagh EG. On the influence of patient-specific material properties in computational simulations: A case study of a large ruptured abdominal aortic aneurysm. *International Journal for Numerical Methods in Biomedical Engineering*. 2013; 29:150–164. [PubMed: 23345202]
21. Wilson JS, Baek S, Humphrey JD. Importance of initial aortic properties on the evolving regional anisotropy, stiffness and wall thickness of human abdominal aortic aneurysms. *Journal of the Royal Society Interface*. 2012; 9:2047–2058.
22. Toungara M, Orgeas L, Geindreau C, Bailly L. Micromechanical modelling of the arterial wall: Influence of mechanical heterogeneities on the wall stress distribution and the peak wall stress. *Comput. Methods Biomech. Biomed. Eng.* 2013; 16:22–24.
23. Toungara M, Chagnon G, Geindreau C. Numerical analysis of the wall stress in abdominal aortic aneurysm: Influence of the material model near-incompressibility. *J Mech Med Biol*. 2012; 12:1250005.
24. Reeps C, Maier A, Pelisek J, Hartl F, Grabher-Meier V, Wall WA, Essler M, Eckstein HH, Gee MW. Measuring and modeling patient-specific distributions of material properties in abdominal aortic aneurysm wall. *Biomechanics and Modeling in Mechanobiology*. 2013; 12:717–733. [PubMed: 22955570]
25. Polzer S, Gasser TC, Bursa J, Staffa R, Vlachovsky R, Man V, Skacel P. Importance of material model in wall stress prediction in abdominal aortic aneurysms. *Med. Eng. Phys.* 2013; 35:1282–1289. [PubMed: 23434615]
26. Polzer S, Gasser TC, Swedenborg J, Bursa J. The impact of intraluminal thrombus failure on the mechanical stress in the wall of abdominal aortic aneurysms. *European Journal of Vascular and Endovascular Surgery*. 2011; 41:467–473. [PubMed: 21269846]
27. Maier A, Gee MW, Reeps C, Eckstein HH, Wall WA. Impact of calcifications on patient-specific wall stress analysis of abdominal aortic aneurysms. *Biomechanics and Modeling in Mechanobiology*. 2010; 9:511–521. [PubMed: 20143120]
28. Di Martino ES, Bohra A, Vande Geest JP, Gupta N, Makaroun MS, Vorp DA. Biomechanical properties of ruptured versus electively repaired abdominal aortic aneurysm wall tissue. *J Vasc Surg*. 2006; 43:570–576. [PubMed: 16520175]
29. Di Martino ES, Guadagni G, Fumero A, Ballerini G, Spirito R, Biglioli P, Redaelli A. Fluid-structure interaction within realistic three-dimensional models of the aneurysmatic aorta as a guidance to assess the risk of rupture of the aneurysm. *Med Eng Phys*. 2001; 23:647–655. [PubMed: 11755809]

30. Di Martino ES, Vorp DA. Effect of variation in intraluminal thrombus constitutive properties on abdominal aortic aneurysm wall stress. *Ann Biomed Eng.* 2003; 31:804–809. [PubMed: 12971613]
31. Xenos M, Rambhia SH, Alemu Y, Einav S, Labropoulos N, Tassiopoulos A, Ricotta JJ, Bluestein D. Patient-based abdominal aortic aneurysm rupture risk prediction with fluid structure interaction modeling. *Annals of Biomedical Engineering.* 2010; 38:3323–3337. [PubMed: 20552276]
32. Rissland P, Alemu Y, Einav S, Ricotta J, Bluestein D. Abdominal aortic aneurysm risk of rupture-patient specific fsi simulations using anisotropic model. *J. Biomech. Eng.* 2009; 13:031001–031010. [PubMed: 19154060]
33. Scotti C, Shkolnik A, Muluk S, Finol E. Fluid-structure interaction in abdominal aortic aneurysms: Effects of asymmetry and wall thickness. *Biomedical Engineering Online.* 2005; 4:64. [PubMed: 16271141]
34. Bluestein D, Dumont K, De Beule M, Ricotta J, Impellizzeri P, Verhegghe B, Verdonck P. Intraluminal thrombus and risk of rupture in patient specific abdominal aortic aneurysm - fsi modelling. *Comput Methods Biomech Biomed Engin.* 2008; 12:73–81. [PubMed: 18651282]
35. Venkatasubramanian AK, Fagan MJ, Mehta T, Mylankal KJ, Ray B, Kuhan G, Chetter IC, McCollum PT. A comparative study of aortic wall stress using finite element analysis for ruptured and non-ruptured abdominal aortic aneurysms. *European Journal of Vascular and Endovascular Surgery.* 2004; 28:168–176. [PubMed: 15234698]
36. Papaharilaou Y, Ekaterinaris JA, Manousaki E, Katsamouris AN. A decoupled fluid structure approach for estimating wall stress in abdominal aortic aneurysms. *Journal of Biomechanics.* 2007; 40:367–377. [PubMed: 16500664]
37. Wang XH, Li XY. A fluid-structure interaction-based numerical investigation on the evolution of stress, strength and rupture potential of an abdominal aortic aneurysm. *Comput. Methods Biomech. Biomed. Eng.* 2013; 16:1032–1039.
38. Wang XH, Li XY. Computational simulation of aortic aneurysm using fsi method: Influence of blood viscosity on aneurismal dynamic behaviors. *Computers in Biology and Medicine.* 2011; 41:812–821. [PubMed: 21757193]
39. Hsu MC, Bazilevs Y. Blood vessel tissue prestress modeling for vascular fluid-structure interaction simulation. *Finite Elem. Anal. Des.* 2011; 47:593–599.
40. Giuma SKB, Osman K, Kadir MRA. Fluid structure interaction analysis in abdominal aortic aneurysms: Influence of diameter, length, and distal neck. *J. Med. Imaging Health Inform.* 2013; 3:514–522.
41. Vande Geest JP, Sacks MS, Vorp DA. The effects of aneurysm on the biaxial mechanical behavior of human abdominal aorta. *J Biomech.* 2006; 39:1324–1334. [PubMed: 15885699]
42. Holzapfel G, Stadler M, Gasser TC. Changes in the mechanical environment of stenotic arteries during interaction with stents: Computational assessment of parametric stent designs. *Journal of Biomechanical Engineering-Transactions of the Asme.* 2005; 127:166–180.
43. Holzapfel GA, Gasser TC. Computational stress-deformation analysis of arterial walls including high-pressure response. *International Journal of Cardiology.* 2007; 116:78–85. [PubMed: 16822562]
44. Holzapfel GA, Gasser TC, Ogden RW. Comparison of a multi-layer structural model for arterial walls with a fung-type model, and issues of material stability. *Journal of Biomechanical Engineering-Transactions of the Asme.* 2004; 126:264–275.
45. Holzapfel GA, Gasser TC, Stadler M. A structural model for the viscoelastic behavior of arterial walls: Continuum formulation and finite element analysis. *European Journal of Mechanics a-Solids.* 2002; 21:441–463.
46. Holzapfel GA, Sommer G, Gasser CT, Regitnig P. Determination of layer-specific mechanical properties of human coronary arteries with nonatherosclerotic intimal thickening and related constitutive modeling. *American Journal of Physiology-Heart and Circulatory Physiology.* 2005; 289:H2048–H2058. [PubMed: 16006541]
47. Doyle BJ, Cloonan AJ, Walsh MT, Vorp DA, McGloughlin TM. Identification of rupture locations in patient-specific abdominal aortic aneurysms using experimental and computational techniques. *Journal of Biomechanics.* 2010; 43:1408–1416. [PubMed: 20152982]

48. de Putter S, Wolters BJ, Rutten MC, Breeuwer M, Gerritsen FA, van de Vosse FN. Patient-specific initial wall stress in abdominal aortic aneurysms with a backward incremental method. *J Biomech.* 2006; 40:1081–1090. [PubMed: 16822515]
49. Wolters BJ, Rutten MC, Schurink GW, Kose U, de Hart J, van de Vosse FN. A patient-specific computational model of fluid-structure interaction in abdominal aortic aneurysms. *Med Eng Phys.* 2005; 27:871–883. [PubMed: 16157501]
50. Holzapfel GA, Gasser TC, Ogden RW. A new constitutive framework for arterial wall mechanics and a comparative study of material models. *Journal of Elasticity.* 2000; 61:1–48.
51. Roach MR, Burton AC. The reason for the shape of the distensibility curves of arteries. *Can J Biochem Physiol.* 1957; 35:681–690. [PubMed: 13460788]
52. Fillinger MF, Raghavan ML, Marra SP, Cronenwett JL, Kennedy FE. In vivo analysis of mechanical wall stress and abdominal aortic aneurysm rupture risk. *J Vasc Surg.* 2002; 36:589–597. [PubMed: 12218986]
53. Chuong CJ, Fung YC. On residual stresses in arteries. *J Biomech Eng.* 1986; 108:189–192. [PubMed: 3079517]
54. Rodriguez JF, Ruiz C, Doblare M, Holzapfel GA. Mechanical stresses in abdominal aortic aneurysms: Influence of diameter, asymmetry, and material anisotropy. *J Biomech Eng.* 2008; 130:021023. [PubMed: 18412510]
55. Sussman T, Bathe KJ. A finite-element formulation for nonlinear incompressible elastic and inelastic analysis. *Computers & Structures.* 1987; 26:357–409.
56. Di Martino E, Mantero S, Inzoli F, Melissano G, Astore D, Chiesa R, Fumero R. Biomechanics of abdominal aortic aneurysm in the presence of endoluminal thrombus: Experimental characterisation and structural static computational analysis. *Eur J Vasc Endovasc Surg.* 1998; 15:290–299. [PubMed: 9610340]
57. Bluestein D, Alemu Y, Avrahami I, Gharib M, Dumont K, Ricotta JJ, Einav S. Influence of microcalcifications on vulnerable plaque mechanics using fsi modeling. *J Biomech.* 2008; 41:1111–1118. [PubMed: 18258240]
58. Vengrenyuk Y, Cardoso L, Weinbaum S. Micro-ct based analysis of a new paradigm for vulnerable plaque rupture: Cellular microcalcifications in fibrous caps. *Mol Cell Biomech.* 2008; 5:37–47. [PubMed: 18524245]
59. Rivlin RS. Large elastic deformations of isotropic materials .1. Fundamental concepts. *Philosophical Transactions of the Royal Society of London Series a-Mathematical and Physical Sciences.* 1948; 240:459–508.
60. Olufsen MS, Peskin CS, Kim WY, Pedersen EM, Nadim A, Larsen J. Numerical simulation and experimental validation of blood flow in arteries with structured-tree outflow conditions. *Annals of Biomedical Engineering.* 2000; 28:1281–1299. [PubMed: 11212947]
61. Vande Geest JP, Wang DH, Wisniewski SR, Makaroun MS, Vorp DA. Towards a noninvasive method for determination of patient-specific wall strength distribution in abdominal aortic aneurysms. *Ann Biomed Eng.* 2006; 34:1098–1106. [PubMed: 16786395]
62. 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. [PubMed: 10768396]
63. Xenos M, Alemu Y, Zamfir D, Einav S, Ricotta JJ, Labropoulos N, Tassiopoulos A, Bluestein D. The effect of angulation in abdominal aortic aneurysms: Fluid-structure interaction simulations of idealized geometries. *Medical & Biological Engineering & Computing.* 2010; 48:1175–1190. [PubMed: 21088917]
64. Ferruzzi J, Vorp DA, Humphrey JD. On constitutive descriptors of the biaxial mechanical behaviour of human abdominal aorta and aneurysms. *Journal of the Royal Society Interface.* 2011; 8:435–450.
65. Gasser TC, Gallinetti S, Xing X, Forsell C, Swedenborg J, Roy J. Spatial orientation of collagen fibers in the abdominal aortic aneurysm's wall and its relation to wall mechanics. *Acta Biomater.* 2012; 8:3091–3103. [PubMed: 22579983]

66. Martufi G, Christian Gasser T. Review: The role of biomechanical modeling in the rupture risk assessment for abdominal aortic aneurysms. *J Biomech Eng.* 2013; 135:021010. [PubMed: 23445055]
67. Speelman L, Schurink GW, Bosboom EM, Buth J, Breeuwer M, van de Vosse FN, Jacobs MH. The mechanical role of thrombus on the growth rate of an abdominal aortic aneurysm. *J Vasc Surg.* 2010; 51:19–26. [PubMed: 19944551]
68. Kim HJ, Vignon-Clementel IE, Figueroa CA, LaDisa JF, Jansen KE, Feinstein JA, Taylor CA. On coupling a lumped parameter heart model and a three-dimensional finite element aorta model. *Annals of Biomedical Engineering.* 2009; 37:2153–2169. [PubMed: 19609676]

Figure 1. Coronal (a) and axial (b) views of the CT data are overlaid by the reconstructed 3D geometry. (c) 3D reconstruction of a ruptured aneurysm (rAAA).

Figure 2.

Representative cases from each group, normals (N3 & 4), AAAs (AAA7 & 8) and rAAAs (rAAA6 & 8), see Table 2. (a) Coronal cross-sectional view of velocity vector fields 0.15 s after peak systole. (b) Von Mises stress in the aortic wall for the isotropic material model formulation. (c) RPI for the pathological cases.

Figure 3.

The graphs show the maximum von Mises stress and maximum RPI versus maximum aortic diameter at peak systole for all the subjects (normal aortas: yellow, non-ruptured AAAs: orange, ruptured AAAs: red).

Figure 4.

FSI simulations of four representative contained rAAAs (one from each diameter group studied, from left to right, rAAA1, rAAA3, rAAA5 and rAAA8, see Table 2 for diameters and maximum stresses and Appendix for more information). The arrows indicate the actual rupture location (known a priori from ER CT scans). Although there are larger regions that may appear with high stresses, sometimes small areas with actual higher stress concentrations are more prone to rupture due to geometrical characteristics or other factors such as small-Ca embedded in the aortic wall.

Figure 5.

Box and Whisker plots for maximum von Mises stress at (a) peak systole and (b) mean arterial pressure (MAP) for the three different groups, $n=24$ (8 normals / 8 AAAs / 8 rAAAs) in MPa.

Table 1

Material properties for the normal and pathological wall (isotropic/anisotropic) and calcifications used in the FSI simulations

Material coefficients	<i>Isotropic coefficients</i>				<i>Anisotropic coefficients</i>			
	C_1 [Pa]	C_2 [Pa]	D_1 [Pa]	D_2	k_1 [Pa]	k_2	a_a°	a_b°
Physiological Wall (isotropic)	4,444	90,695	26.785	29.48	--	--	--	--
Pathological Wall (isotropic)	8,888	164,900	48.7	53.46	--	--	--	--
Pathological Wall (anisotropic)	8,888	164,900	48.7	53.46	1,886	94.75	5°	265°
Calcification	92,000		36,000	2.0	--			

Table 2

Geometrical and mechanical parameters (maximum von Mises and maximum principal axis, p_1 , stresses) for the normal and pathological aortas (nor-ruptured AAA and ruptured AAA) at peak systole and during mean arterial pressure (MAP). The maximum value of RPI is reported for the pathological cases. (see Appendix for more details)

Subject	Sex	Max diam. (cm)	ILT max thickness (cm)	Peak max. systolic wall stress (isotropic, von Mises, MPa)	Peak max. wall stress at MAP (isotropic, von Mises, MPa)	Peak max. systolic wall stress (anisotropic, p_1 stress, MPa)	RPI
N1	Female	1.63	--	0.350	0.338	0.370	--
N2	Female	1.80	--	0.440	0.297	0.540	--
N3	Male	1.97	--	0.283	0.207	--	--
N4	Male	2.60	--	0.403	0.331	--	--
N5	Female	1.93	--	0.404	0.314	--	--
N6	Female	1.60	--	0.317	0.260	--	--
N7	Male	1.29	--	0.348	0.264	--	--
N8	Male	1.83	--	0.440	0.292	--	--
AAA1	Male	3.88	2.19	0.430	0.331	--	0.446
AAA2	Male	3.83	3.51	0.500	0.234	--	0.440
AAA3	Male	4.60	2.01	0.500	0.423	0.650	0.493
AAA4	Male	5.10	2.17	0.480	0.368	--	0.390
AAA5	Male	5.73	--	1.360	0.961	--	0.693
AAA6	Male	6.40	1.99	0.506	0.354	--	0.539
AAA7	Male	7.10	2.76	0.664	0.472	--	0.660
AAA8	Male	7.60	3.45	0.540	0.412	--	0.650
rAAA1	Male	6.31	1.49	1.014	0.683	--	1.222
rAAA2	Male	6.55	2.36	1.905	0.920	--	0.969
rAAA3	Male	7.46	2.35	0.815	0.526	--	0.818
rAAA4	Male	7.52	2.38	0.640	0.528	--	0.752
rAAA5	Male	7.80	2.64	2.100	1.990	2.170	0.950
rAAA6	Male	8.10	3.29	1.214	0.931	--	0.874
rAAA7	Male	10.30	4.02	1.088	0.862	--	1.339
rAAA8	Male	10.60	2.79	1.090	0.850	1.370	0.800