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The Role of Geometric Parameters in the Prediction of Abdominal Aortic Aneurysm Wall Stress

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KEYWORDS
Wall stress;
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Abstract *Objective:* To study the correlation between peak wall stress (PWS) and abdominal aorta aneurysm (AAA) geometric parameters in the presence of intraluminal thrombus (ILT).
Design: Computational study using finite element analysis.
Material: AAA models were created by three-dimensional (3D) reconstruction of *in vivo* acquired computed tomography (CT) images from 19 patients.
Methods: PWS was evaluated in the presence and absence of ILT. ΔPWS% represents the percentage change in PWS in the presence of ILT. The 3D lumen centrelines were extracted, and the values of torsion, tortuosity and mean curvature were estimated.
Results: A positive correlation was observed between ΔPWS% and relative ILT volume ($P = 0.03$). PWS in the presence of ILT significantly correlated only with the degree of centerline tortuosity ($P = 0.003$) and maximum diameter ($P < 0.0001$). The optimal predictive model for PWS in the presence of ILT was estimated to contain both maximum diameter and centreline tortuosity.
Conclusions: Specific geometric parameters in AAA models in the presence of ILT could serve as potential predictors of elevated PWS. PWS correlated significantly with the maximum diameter and the degree of centreline tortuosity. Centreline tortuosity may become a useful addition to maximum diameter in the decision-making process of AAA treatment.

Introduction

It has been postulated that aneurysm peak wall stress (PWS) may be superior to diameter in differentiating patients with abdominal aortic aneurysms (AAAs), who will experience

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Table 1 Patient and aneurysm characteristics.

Case number	Sex	Cigarette use	Family history for AAA	Concomitant diseases	Max Transverse Diameter (cm)	PWS - ILT (N/cm^2)	PWS + ILT (N/cm^2)	PWS reduction (%)	ILT (%)
001	Male	+		HT, CHL	5.0	30	20	33	54
002	Male	+		HT, CHL	5.0	20	14	30	51
003	Male	+		CHL	5.0	23	20	15	43
004	Male	+	±		5.1	40	20	50	78
005	Male	+		HT, CHL, DM	5.2	40	30	25	54
006	Male	+		DM	5.5	25	20	20	48
007	Male	+		COPD	5.5	34	28	17	46
008	Male	+		HT, CHL, CAD	6.0	40	20	50	72
009	Male	+			6.2	45	30	33	57
010	Male	+		HT, CHL	6.8	53	33	37	82
011	Male	+		CHL, COPD	8.3	45	33	26	71
012	Male	+		CAD	8.5	40	30	25	45
013	Male	+		HT	8.5	50	45	10	45
014	Male	+		HT, CHL, DM, CAD	8.8	45	32	26	42
015	Male	+		CHL,	9.2	44	33	25	37
016	Male	+		HT, CHL	10.0	58	42	28	59
017	Male	+		COPD	11.0	43	38	12	55
018	Male	+		HT, CHL, CAD	11.3	90	45	50	45
019	Male	+		HT, COPD, DM	12.0	58	34	41	52
Mean					**7.5**	**43.3**	**29.8**	**29.1**	**54.5**
SD (±)					**2.4**	**15.6**	**9.0**	**12.3**	**12.7**

t-test PWS -ILT vs +ILT: ***p: .00001***

PWS: Peak Wall Stress; ILT: Intraluminal Thrombus; AAA: Abdominal Aortic Aneurysm; HT: Hypertension; CHL: elevated blood cholesterol; DM: Diabetes Mellitus; CAD: Coronary Artery Disease; COPD: Chronic Obstructive Pulmonary Disease. Patients with hypertension were receiving treatment and were normotensive.

a catastrophic outcome, in terms of rupture.[1] The evaluation of PWS values is achieved by using the finite element analysis (FEA) method, which was first applied to determine wall stress in idealised two-dimensional geometry AAA models[2] and later to realistic three-dimensional (3D) geometries, obtained from computed tomography (CT) data.[3] This was necessary since previous studies have shown that simple geometric measures (e.g., AAA volume, maximum radius, maximal wall distention, ratio of greatest anteroposterior diameter to transverse diameter and local radii of curvature) are unreliable in predicting AAA stresses.[4,5]

Despite the pathophysiologic interest of PWS, many clinicians question its clinical utility, advocating that the computational difficulty in assessing PWS values and distribution prohibits its everyday clinical practice, since this requires sophisticated software and highly qualified personnel. So, the need to shift the research interest to more easily identified geometric parameters has emerged, since the role of geometric characteristics as significant predictors of PWS and subsequent risk of rupture or tendency to distension, has been recently described. Giannoglou et al. reported that the mean centreline curvature in AAA models without thrombus significantly correlated with PWS.[6] More recently, Doyle et al. and Pappu et al. reported on the importance of AAA asymmetry and tortuosity index as useful adjuncts to diameter for a surgical intervention guide.[7,8]

The task of the present study was to investigate whether a relationship existed between PWS values and specific geometric parameters in patient-specific AAA models, in the presence of intraluminal thrombus (ILT).

Materials and Methods

Nineteen patients with infrarenal aneurysms were included in this study. The AAA maximum diameters ranged from 5 to 12 cm. Patient and aneurysm characteristics are shown in Table 1. None of the patients experienced clinical signs of rupture, nor was there any imaging sign in the CT analysis implying AAA rupture. None of the patients had an inflammatory aneurysm. All patients underwent surgical or endovascular treatment within 2 weeks of the CT examination. Full local ethics committee approval was obtained for our study (University of Crete, Medical School).

Details of our methodology have been previously reported.[9] In brief, information on the 3D AAA realistic geometric configuration was extracted *in vivo* by contrast-enhanced high-resolution spiral CT angiography (Sensation 16, Siemens, Erlagen, Germany), where a 3D reconstruction of the outer and inner lumen were created.[10] Geometric features of the AAA and its intraluminal thrombus were estimated using our previously reported methodology.[9] Both the ILT and the AAA wall were assumed to be homogeneous, incompressible and isotropic materials.

To account for the AAA wall properties, we used the previously described model introduced by Raghavan et al.[2,11] The discretisation of the AAA 3D wall surface

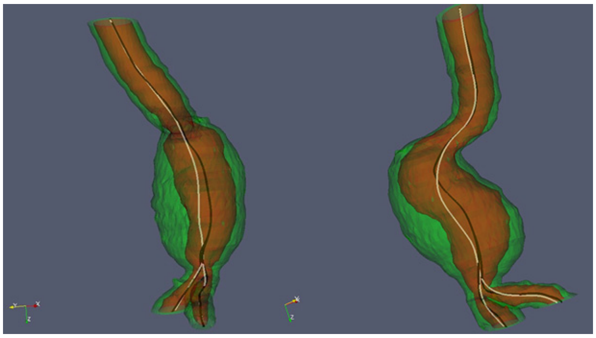

Figure 1 AAA reconstructed models with lumen centreline in the presence (yellow color) and absence (black color) of intraluminal thrombus.

geometry into a finite number of elements for FEA analysis was generated using ANSA (Beta CAE systems, Thessaloniki, Greece). This 3D geometry for each patient is divided into a finite number of elements (FEA analysis). The AAA model assembly also included the ILT solid part, which was discretised using $30-50 \times 10^3$ linear tetrahedral/ hybrid elements.[9] The values of PWS (von Mises stress) in each AAA model were evaluated separately in the presence and absence of intraluminal thrombus with well-validated FEA software ANSYS v 6.1 (Ansys Inc., Canonsburg, PA, USA).[9]

Thrombus volume estimation

The description files of external and internal surface geometry were used for calculating geometry volume with Amira 4 (Visage Imaging Inc., Andover, MA, USA). The aortic neck and the common iliac arteries of the AAA model were excluded, thus only the volume of the aneurysm sac was calculated. The procedure was then repeated to reconstruct the lumen surface of the aneurysm and estimate the lumen volume. The difference between the external and internal volume computation is referred to as the thrombus volume (ILT) and can be further expressed as percentage (%) of the sac volume.[9]

Loading and constrains

The same mean systolic pressure (mmHg) of 120 mmHg was used for all AAA models. The outer surface of the AAA was considered load-free, with no residual stresses, as previously reported by Wang at al.[12] The aneurysm wall thickness was considered uniform at 2 mm (the standard reported value). Our FEA models were constrained proximally from the border of the highest renal artery down to the common iliac arteries.[9]

Extraction of lumen centrelines and estimation of geometric parameters values

The reconstructed 3D lumen of the models in the presence and absence of ILT were processed separately using the VMTK software.[13] The centrelines were extracted for each model, respectively, taking into account the AAA segment from the level just below the lowest renal artery, to the caudal end of the aneurysm sac (Fig. 1).

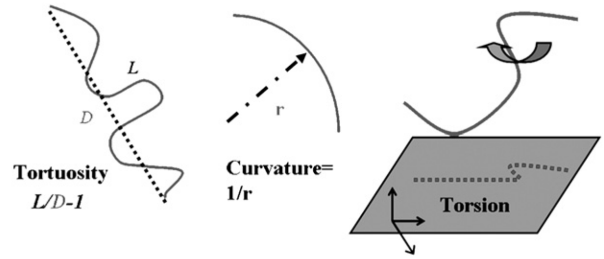

Figure 2 Schematic visualization of curvature, torsion and tortuosity. Torsion is measured in 1/cm^2, curvature is measured in 1/cm, whereas tortuosity is an absolute number.

The values of mean curvature and torsion were calculated along the centreline, for each model in the presence and absence of ILT. The visual representation of each parameter is shown in Fig. 2. Tortuosity expresses the fractional increase in length of a tortuous vessel in relation to the imaginary straight line and has been described elsewhere.[14]

Statistical analysis

Data were entered into a customised database and were analysed using SAS (ver. 9.2) and R (ver. 2.8.0) statistical packages.[15,16] To evaluate the strength of linear associations between PWS values and any of the geometric parameters, the statistical significance of Spearman's correlation coefficients was examined. Correlations with a $P < 0.05$ were considered significant.

A linear regression model building procedure was employed to reveal the optimal set of explanatory variables for a predictive model for PWS in the presence of thrombus. The dependent variable in the regression model was PWS in the presence of thrombus and the set of possible explanatory variables for the regression model included maximum diameter, internal tortuosity, torsion, curvature and relative ILT volume. Optimal regression models were estimated according to three criteria: the adjusted goodness-of-fit criterion (adjusted R^2); Mallows C_p and Amemiya's prediction error criterion. The model with the lowest C_p value, approximately equal to P, is the most 'adequate' model.

Results

PWS values in the presence and absence of ILT for each aneurysm model and the corresponding reduction percentages (ΔPWS%) are depicted in Table 1. It can be observed that the presence of ILT correlated with a significant reduction of PWS ($P = 0.00001$). Statistically significant positive correlation was observed between ΔPWS% and relative ILT volume (Spearman's r: 0.50, $P = 0.03$). The values of curvature, torsion and tortuosity for the extracted AAA lumen centreline were calculated both in the presence and in the absence of thrombus (Table 2).

No evidence of a linear association was observed between PWS values (with ILT included) and ILT% (Spearman's $r = 0.08$, $P = 0.73$, Fig. 3A). An examination of the linear associations between the geometric variables (calculated in

Table 2 Geometric characteristics of AAA centrelines.

Case number	Ext curv (1/cm)	Ext tortion (10^{-2}/cm^2)	Ext tortuosity	Int curv (1/cm)	Int tortion (10^{-2}/cm^2)	Int tortuosity
001	0.11	0.21	0.04	0.14	0.19	0.03
002	0.10	0.01	0.03	0.18	0.41	0.03
003	0.14	0.25	0.06	0.13	0.62	0.04
004	0.19	0.27	0.13	0.15	0.31	0.07
005	0.10	0.56	0.06	0.14	0.27	0.04
006	0.15	0.31	0.53	0.17	0.19	0.05
007	0.24	0.23	0.25	0.25	0.38	0.26
008	0.18	0.08	0.12	0.20	0.23	0.11
009	0.06	0.14	0.03	0.08	0.54	0.03
010	0.11	0.96	0.07	0.15	0.11	0.06
011	0.11	0.07	0.07	0.26	0.16	0.11
012	0.13	0.08	0.06	0.20	0.37	0.09
013	0.17	0.24	0.10	0.33	0.12	0.32
014	0.14	0.12	0.12	0.18	0.28	0.16
015	0.17	0.09	0.11	0.16	0.15	0.13
016	0.10	0.09	0.05	0.14	0.12	0.07
017	0.14	0.09	0.16	0.11	0.72	0.15
018	0.14	0.34	0.12	0.22	0.25	0.33
019	0.09	0.04	0.08	0.13	0.01	0.23
mean	**0.14**	**0.22**	**0.12**	**0.17**	**0.29**	**0.12**
SD	**0.04**	**0.22**	**0.11**	**0.07**	**0.19**	**0.10**

Ext: External, refers to geometric parameters calculated in 3D models in the absence of ILT. **Int:** Internal, refers to geometric parameters calculated in 3D models in the presence of ILT.

the presence of thrombus) and PWS in models with ILT revealed a strong positive relationship (Spearman's $r = 0.65$, $P = 0.003$) between PWS and internal tortuosity (Fig. 3B). In addition, a strong linear correlation was observed between maximum transverse diameter and internal tortuosity (Spearman's $r = 0.72$, $P = 0.01$, Fig. 3C). On the contrary, no evidence in favour of a linear association was observed for curvature (Spearman's $r = 0.1$, $P = 0.66$, Fig. 3D) and torsion (Spearman's $r = -0.44$, $P = 0.06$, Fig. 3E).

PWS values when ILT was included were found to strongly correlate with the maximum diameter (Spearman's $r = 0.88$, $P < 0.0001$, Fig. 4). A regression model selection procedure was then applied to investigate whether a better prediction of PWS can be achieved compared with the maximum diameter alone. Evaluation of the above statistical criteria for all possible sets of combinations of the explanatory variables revealed that the optimal predictive model included both maximum diameter and internal tortuosity. In Table 3, the relevant model selection procedure is depicted where one can observe that the model that includes maximum diameter alone as a predictive variable is the second best model under the C_p criterion. We were able to find that a linear regression model that included both maximum diameter and internal tortuosity explained approximately 68.5% of the variability in observed PWS values when ILT was included whereas approximately 63.5% of the variability was explained by maximum diameter alone. After estimation of the corresponding regression coefficients by least squares, the optimal predictive model can be formulated as follows: $\boldsymbol{PWS = 8.791 + 2.395 \times MaxDiam + 25.292 \times Int\ Tortuosity}$.

Discussion

The wall stress estimation with the FEA technique has been extensively used through the past decade, taking into account a well-known mathematical model that describes the biomechanical properties of the AAA wall.[2] Studies on idealised AAA models with ILT[17,18] and on patient-specific 3D models[12,19] have been published. Construction of 3D patient-specific reconstructed models has been achieved, as well as software programs that provide a robust and objective way of constructing model centrelines, providing standardisation of geometric definitions for future studies.[13,14]

The only geometric parameter in our study which showed a positive linear correlation with PWS in models with ILT was internal tortuosity (Fig. 3B). Geometric characteristics may help to estimate PWS values, since PWS analysis requires experienced staff and considerably higher computational cost.[20]

We found that PWS is reduced by the presence of ILT (Table 1). The observed statistically significant linear association between ΔPWS% and relative ILT volume is in agreement with the results of a recent study in a group of 20 patients by Li et al.[19] When we examined the PWS values against ILT% (in the ILT-integrating AAA reconstructed models), no significant linear correlation was observed. Although this seems to contradict the results of the former study, we think that this difference could simply mirror the influence that geometric factors can exert on PWS evaluation and, thus, on its resulting relations. This could, in fact, imply that ILT does not reliably affect PWS and that other factors (like geometry) affect PWS more than the presence or absence of ILT.

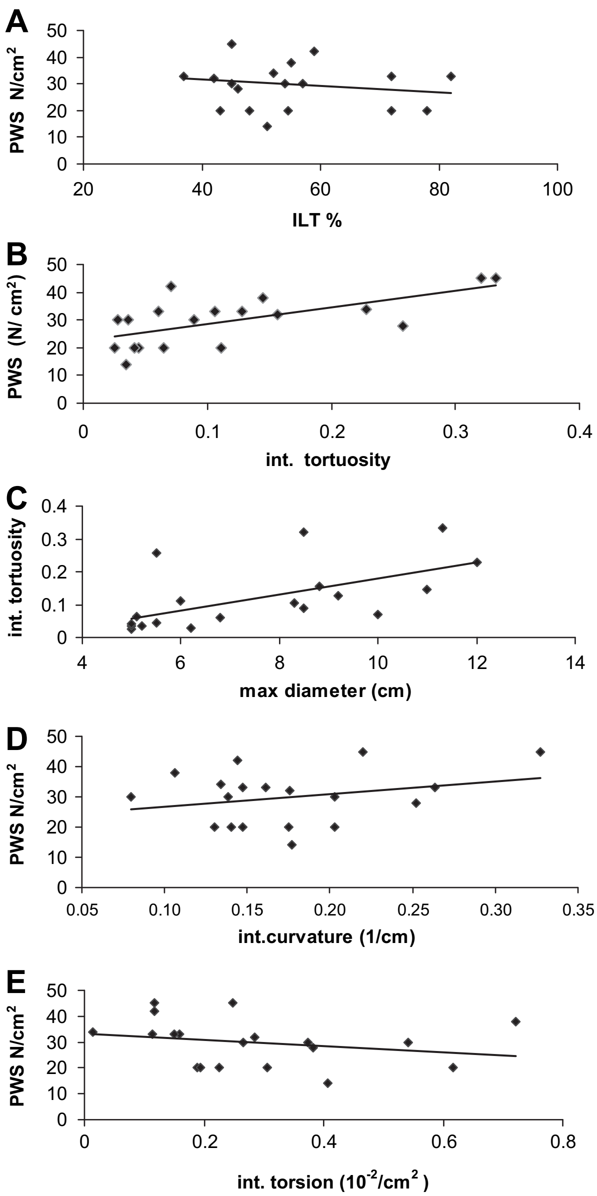

Figure 3 A. PWS values (ILT included) against the relative ILT volume. No correlation was observed (Spearman's $r = .08$; $P = .73$). B. PWS values (ILT included) against internal tortuosity in models with ILT included. Linear correlation was observed (Spearman's $r = .65$, $P = .03$). C. A strong linear correlation was observed between maximum transverse diameter and internal tortuosity (Spearman's $r = .72$, $P = .01$). The 3 outliers may be attributed to the highly asymmetric and non-uniform distribution of the intraluminal thrombus that characterizes these specific cases. D. PWS values (ILT included) against internal curvature in models with ILT included. No correlation was observed (Spearman's $r = .10$, $P = .66$). E. PWS values (ILT included) against internal torsion in models with ILT included. No positive linear correlation was observed (Spearman's $r = -.44$, $P = .06$).

The tortuosity of the centreline in our models was greatly dependent on the amount and the distribution of thrombus, the latter greatly influencing the PWS values and distribution. For this reason, we strongly believe that not only ILT should be incorporated in AAA models but also tortuosity reflects the issues about ILT, as mentioned before.

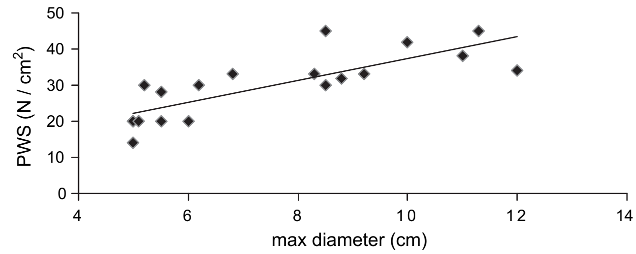

Figure 4 PWS values (ILT included) against max diameter. Strong linear correlation was observed (Spearman's r: .88, $P < .0001$).

Studying 15 patient-specific AAA models without the integration of ILT, Doyle et al. showed that PWS strongly correlated with the maximum diameter as well as with the centreline asymmetry, the latter being defined as the perpendicular distance from the proximal and distal points of the centreline to a defined point of the centreline.[8] It is notable, however, that in 11 of their 15 AAAs, a significant correlation was found between asymmetry and diameter. Therefore, if diameter strongly correlated with peak stress, then asymmetry would also score high. We made the same observation concerning maximum diameter and centreline internal tortuosity. So, the next step was to examine whether these two parameters, when used simultaneously, could improve the ability to better predict PWS values. By using a linear regression model that included both maximum diameter and internal tortuosity in our study, we were able to explain 68.5% of the variability in PWS values, whereas 63.5% of the variability was explained by maximum diameter alone. Although a difference of only 5% may seem quite small, this could be a motivation for future large-scale studies, controlling whether internal tortuosity of greater than some specific value would be associated with future AAA rupture regardless of size.

Risk stratification of AAA rupture is thought to be a multifactorial process including biological, biochemical and biomechanical factors.[21,22] The simple observation that not all AAAs rupture at a specific diameter indicates that other patients or aneurysm-specific variables also affect rupture risk. In a multivariate analysis, Cronenwett et al. observed that increased initial diameter, hypertension and chronic obstructive pulmonary disease (COPD) were independently predictive of rupture in patients with small AAAs.[23] Smoking was identified as a risk factor for rupture in a study of mail civil servants in England, where the relative risk of death from AAA rupture increased 4.6-fold for cigarette smokers, 2.4-fold for cigar smokers and 14.6-fold for smokers of hand-made cigarettes.[24] Important relative new information concerning AAA rupture risk has been obtained from the UK Small Aneurysm Trial data. In a cohort of 2257 patients with a 4.0—5.5 cm AAAs, the relative risk of rupture increased by female gender (3.0 ×), current smoking (1.5 ×), worse COPD (0.6 × per L FEV1) and higher mean arterial pressure (1.02 × per mmHg).[25] Similarly, a positive family history of AAA also appears to increase rupture risk.[26] In our study, all patients were male,

Table 3 Explanatory variables included in a predictive model for PWS values calculated in the presence of thrombus. Sets of variables appear as a decreasing sequence, with respect to the values of model fitting criteria.

Variables in model	Adjusted R^2	Mallows C_p	Amemiya's Prediction Criterion
Max-diam Int-Tortuosity	.65	.46	.43
Max-diam	.61	.53	.45
Max-diam Int-Curvature	.64	.58	.44

all were smokers and only one of these reported a positive family history of AAA in a first-degree relative. Although there is no precise formula that incorporates the risk factors described above to calculate exact rupture risk, the surgeon should use those in his decision-making process in the everyday clinical practice. In our study, emphasis was given only to aneurysm-specific variables that may affect AAA wall stress.

We believe that our effort to depict the importance of geometry on PWS determination by altering the ILT diminishing effect underlines the need for further studies of larger scale, taking into consideration certain geometric factors as predictors of AAA rupture. Nonetheless, one should also take into consideration that predicting PWS without predicting wall failure, one cannot accurately predict rupture.

Study limitations

To perform PWS analysis, we used static structural instead of fluid structure interaction models. Although the use of the latter model can slightly improve the accuracy of the results;[27] however, both models have been shown to resolve the maximum stress locations equally well.[20]

Systolic pressure loading

In our study, we used standard mean systolic pressure of 120 mmHg in our models. This was done because studying the effect of the amount of thrombus and geometry in our models under different individual pressure limits (i.e., having a second variable parameter in our study) would obscure the results of our observations.

Wall thickness

The wall thickness of a realistic AAA varies regionally, from 0.23 mm to 4.26 mm at a calcified site.[28] The heterogeneity in wall thickness can affect PWS values.[27] However, since thorough recording of individual wall thickness is not currently possible to perform in everyday practice, as imaging process generally lacks the sensitivity needed, we used a uniform wall thickness of 2 mm, as commonly reported.

Material properties

The thrombus model was considered isotropic, elastic, homogeneous and incompressible. Population mean parameters for ILT material characteristics can be accurately used to reasonably estimate the wall stresses in patient-specific AAA models.[11,29,30] As previously discussed,[9] using the above simple elastic model for the ILT in our study is sufficient in highlighting the variation in the effect of ILT distribution on AAA's wall stress associated with AAA size and shape.

The aneurysm wall was considered incompressible, homogeneous, hyperelastic, isotropic and pressure unloaded.[2] We realise that the assumption of zero stress in the diastolic state is a simplification that can influence the computed wall stress distribution.[31]As discussed in our previous paper,[9] it is difficult to conclude what would the impact of this model simplification be on our results and therefore we have adopted the zero-residual stress model in our study.

It is important to note that an anisotropic wall material model has been recently described.[32] When those models were compared with the isotropic simulations, there were similar displays of maximum stress contours, although the anisotropic simulations displayed larger stress values over larger areas. Further studies are required to investigate the utility of the anisotropic model.

Moreover, our model does not take into consideration the effect of the aneurysm wall calcification, which has been reported to modify the stress values.[19] This issue still remains under investigation and comparisons of larger scale are needed to delineate the importance of the utility of the initial finding.

Geometry of the bifurcated branches

Our models included AAA neck, the lumen of the sac (with or without ILT) and the corresponding centrelines. More accurate results for the relations mentioned above could be provided if the influence of the bifurcated iliac vessels on the magnitude of PWS but, more importantly, its distribution, were put under evaluation, with respect to their bifurcation, planarity and asymmetry angles. Future studies, taking into account newly developed sophisticated techniques of automated 3D reconstruction of AAA geometry,[33] may be able to determine the effect of the aortic bifurcation on PWS.

Conclusion

In realistic patient-specific AAA cases, we have estimated how PWS relates with specific AAA geometric parameters such as maximum diameter, curvature, torsion and tortuosity. Statistical analysis confirmed that maximum diameter significantly influenced PWS and that tortuosity may also affect PWS values in the same direction. Evaluation of AAA centreline tortuosity may become a useful addition to maximum diameter in the decision-making process of AAA treatment. Certainly, the suggested model requires further study.

Conflict of Interest

None.

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