Effects of aspect ratio, wall thickness and hypertension in the patient-specific computational modeling of cerebral aneurysms using fluid-structure interaction analysis

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ABSTRACT

Intracranial aneurysm is a pathological dilatation of the cerebral artery which can lead to high mortality rate upon rupture. The aspect ratio (AR) of an aneurysm, being the ratio of the height to neck width, is an important factor in estimating the likelihood of aneurysm rupture in clinical practice. AR will generally increase while the aneurysm grows. Clinical observations over the years show that aneurysms with larger AR usually exhibit higher rupture risk. The goal of the current study is to conduct Fluid-Structure Interaction (FSI) analyses to provide quantitative estimates on the importance of AR, wall thickness ($t_w$) and hypertension. The effects of varying AR and $t_w$ on the hemodynamics, wall stress and displacement will be studied based on patient-specific models. Both sidewall and bifurcation aneurysms are investigated. There is a significant increase in the wall stress at the aneurysmal dome (the location in an aneurysm where rupture is commonly observed clinically) when the AR increases and $t_w$ decreases due to the aneurysm growth process. Furthermore, these investigations are repeated for patients with hypertension (high blood pressure) conditions. The increase in the wall stress due to hypertension for models with higher ARs is more dramatic. The clinically observed feature of higher rupture risk of aneurysms with larger AR is thus supported quantitatively.

1. Introduction

Abnormal dilation of the artery, termed aneurysm, can be life-threatening. Rupture of an intracranial aneurysm (IA) can lead to massive internal bleeding in the subarachnoid space. The occurrence rate of IA is 2\% to 5\% in the population (Humphrey & Taylor, 2008) and aneurysm rupture also leads to high mortality rate (Sforza, Putman, & Cebral, 2009). A typical geometric parameter of the aneurysm is the aspect ratio (AR) which is defined as the ratio of the aneurysm height to the equivalent diameter (\(=\)circumference/$\pi$) of the aneurysm neck. Clinical analysis reported that aneurysms with AR greater than 1.6 are prone to rupture (Ujiie, Tamano, Sasaki, & Hori, 2001). Several types of endovascular surgical treatment including coiling and flow diverter stenting are available for mitigating the risk of rupture.

The underlying mechanism of aneurysm rupture is complicated and not well understood. Intensive computational studies have been performed to assess the rupture risk of an IA and the post-treatment response (Ahmed, Šutalo, Kavnounidias, & Madan, 2011; Berg et al., 2015; Ford, Lee, Lownie, Holdsworth, & Steinman, 2008a; Nair et al., 2016; Tang et al., 2015; Varble, Xiang, Lin, Levy, & Meng, 2016; Zhang, Chong, & Qian, 2013). The influence of the geometry of the aneurysm (in particular AR) and the nearby vasculature on the risk of rupture has been investigated computationally and experimentally (Hoi, Wasserman, Lakatta, & Steinman, 2010; Lai et al., 2016). The hemodynamics inside the aneurysm would play an important role. Computational results have been compared with in vivo magnetic resonance imaging (MRI) measurement and particle imaging velocimetry (PIV) in experiments (Ford et al., 2008b; Rayz et al., 2008). However, many investigations have been conducted based on the rigid wall assumption (Inthavong, Wen, Tu, & Tian, 2009; McGarry, Hitt, & Harris, 2008; Tang, Fan, Cheng, & Chow, 2012). Since the arterial and the aneurysm walls are elastic, taking the wall motion and dilatation into account may provide additional insight on analysing aneurysm rupture risk.
Fluid-structure interaction (FSI) analyses simulate the interaction between fluid and solid domains by incorporating fluid dynamics, structural/solid mechanics as well as the coupling between the fluid and solid domains. Biomechanical factors including arterial and aneurysm geometries, thickness of the aneurysm wall ($t_w$), blood pressure, outflow/inflow conditions and a measure of fluid friction, namely, the wall shear stress (WSS) have been investigated (Torii, Oshima, Kobayashi, Takagi, & Tezduyar, 2011). The arterial and the aneurysm geometries are believed to play a critical role in the process of rupture. A curved parent vessel might be associated with greater risk of aneurysmal wall damage (Ahmed et al., 2011). The effect of AR scaled to the range of 0.3–2.0 has been investigated with FSI using patient models (Long et al., 2015). As AR increases, energy loss per unit aneurysmal volume increases and is used to assess rupture risk (Long et al., 2015). However, the stress of the aneurysmal wall and the spatial variation of such stress have not been reported.

Besides AR, $t_w$ is another critical parameter (Sanchez et al., 2013; Torii, Oshima, Kobayashi, Takagi, & Tezduyar, 2010; Valencia & Solis, 2006). It can influence the dilatational variation of an aneurysm in the cardiac cycle (Sanchez et al., 2013). Moreover, utilizing a pathologically realistic $t_w$ of 0.05 mm can affect the wall displacement and WSS by more than 50% compared to a model with a normal, uniform $t_w$ of 0.3 mm (Torii et al., 2010). Indeed, it can be well-expected that a smaller $t_w$ would lead to larger wall displacement and stress (Valencia & Solis, 2006). FSI analyses utilizing patient-specific $t_w$ have also been performed (Voß et al., 2016). Besides effects due to geometry, dynamical factors like hypertension and pressure gradient also affect the rupture risk (Ahmed et al., 2011; Long et al., 2015; Valencia & Torres, 2017) through changes in the wall stress of the aneurysm and WSS (Ahmed et al., 2011; Lee, Zhang, Takao, Murayama, & Qian, 2013). A comparison between pre-ruptured and unruptured aneurysms has also been undertaken (Lee et al., 2013). The former entities were constructed with imaging data just before rupture. Larger displacement at the dome region, lower WSS and a higher wall stress are observed in the pre-rupture state. However, the effects of AR increase and $t_w$ reduction due to aneurysm growth have not been incorporated in all these previous studies (Ahmed et al., 2011; Lee et al., 2013; Sanchez et al., 2013; Torii et al., 2011; Valencia et al., 2013; Valencia & Torres, 2017).

In the current study four patient-specific aneurysm models, consisting of two sidewall and two bifurcation cases, were used to study how the AR increase and $t_w$ reduction arising from aneurysm scaling would affect the blood hemodynamics and the wall stress. The WSS, wall stress and wall displacement are commonly used to assess the rupture risk as the aneurysm grows. Our results show that all these quantities evolve with the AR increase and $t_w$ reduction in the way that the IA rupture risk becomes higher. It is also noted that an aneurysm with a higher AR after scaling would also exhibit a long-term low WSS scenario under the condition of hypertension, further enhancing the rupture risk.

2. Methods

2.1. Geometric configuration

Four patients with IA were selected for the FSI analysis. The consent of the patients and the approval by the Institutional Review Board of the Hospital were obtained. The morphology of the aneurysm and the nearby vasculature were obtained by standard imaging procedures (Figure 1). For Patient A, computed tomography angiograms (CTAs) were produced by the Toshiba Medical Systems Corporation (in-plane resolution 0.43 mm, slice thickness 0.50 mm) with the aid of a contrast agent. For Patient B, magnetic resonance angiograms (MRAs) were produced by the Signa Excite scanner manufactured by GE Medical Systems (in-plane resolution 0.47 mm, slice thickness 1.00 mm). For Patients C and D, CTAs were produced by the LightSpeed VCT scanner manufactured by the GE Medical Systems (in-plane resolution 0.27 mm, slice thickness 0.63 mm) with the aid of contrast agent. Based on these imaging data, three-dimensional models were constructed by selecting the solid-fluid boundary for every slice in the software Mimics 18.0 (Materialise, Leuven, Belgium) (Tang et al., 2015). These geometric configurations were then exported in STL format, and were smoothed by

Figure 1. Geometric configurations of patient-specific models. Blue arrows indicate the flow direction inside the models.
### Table 1. Information on the patients and geometric configurations.

| Model | Gender | Age | Aneurysm type          | Aspect ratio | Aneurysmal volume (mm³) |
|-------|--------|-----|------------------------|--------------|-------------------------|
| Patient A | F     | 71  | Sidewall Aneurysm     | 1.5          | 938.8                   |
| Patient B | F     | 36  | Sidewall Aneurysm     | 1.9          | 207.8                   |
| Patient C | F     | 61  | Bifurcation Aneurysm  | 1.2          | 538.3                   |
| Patient D | F     | 75  | Bifurcation Aneurysm  | 2.2          | 633.4                   |

SOLIDWORKS 2016 and its reverse engineering add-in ScanTo3D. Since the precision of the imaging data was not sufficient to resolve the aneurysm wall, the wall thickness of the models was assumed to be uniform. Selected information on the patients and the geometric configurations of the aneurysms were provided in Table 1.

### 2.2. The scaling method

When the aneurysm grows, AR increases and $t_w$ reduces. To study the effect of AR and $t_w$ on the blood hemodynamics and the wall stress, the patient-specific aneurysm models were scaled to create the models with higher ARs and lower $t_w$s by noting that expansion of the aneurysm increases monotonically from the neck to the dome during the aneurysm grows (Kroon, 2011) and the $t_w$ of ruptured aneurysms can be as thin as 0.05 mm (Abruzzo et al., 1998). The following scaling procedure was formulated:

1. The necking plane, being the narrowest transverse section of the aneurysm, was visually identified. Normal to the neck defines the longitudinal coordinate $V$ as shown in Figure 2. $V$ is taken as zero at the necking plane.
2. $V_{\text{max}}$, the value of $V$ at the highest point of the dome, was measured.
3. At any $V$ termed $V_c$, the boundary contour of the aneurysm was extracted. The contour was shifted to $V = \alpha V_c$ where $\alpha$ was a scaling factor to be defined in the next step. The contour was also expanded transversely and normal to the contour by a constant offset equal to $(\alpha - 1)$ times the effective diameter of the contour before expansion.
4. There was no expansion below the necking plane, i.e. $\alpha = 1$ for $V < 0$. The factor $\alpha$ increased linearly.

![Figure 2](image)
from unity at \( V = 0 \) to \( \alpha_{\text{max}} \) at \( V = V_{\text{max}}/3 \) and remained at \( \alpha_{\text{max}} \) for \( V > V_{\text{max}}/3 \). \( \alpha_{\text{max}} \) was determined by keeping the tissue volume, equal to the integral of \( t_w \) over the surface area of the aneurysm, constant and \( t_w \) after the scaling to be 50% of that before the expansion.

A constant \( \alpha \) instead of the linearly increasing \( \alpha \) was used for \( V > V_{\text{max}}/3 \), as the morphology of the aneurysm would be seriously distorted otherwise. For instance, a cylindrical aneurysm will become the one aneurysm would be seriously distorted otherwise. For instance, a cylindrical aneurysm will become the one with a much larger dome. By trial and error, \( \alpha_{\text{max}} \) was determined to be 1.28, 1.26, 1.27 and 1.24 whilst the ARs after growth were 1.8, 2.3, 1.5 and 2.6 for the models of Patients A, B, C and D, respectively.

2.3. Governing equations

2.3.1. Fluid model

Computational simulations of fluid motion are often conducted through Eulerian meshes fixed in space. On the other hand, deformations of the solid materials are often considered by Lagrangian meshes which deform with the material. While the treatment of moving boundary/interface is trivial in Lagrangian meshes, the fluid displacement would quickly ruin the mesh quality. The Arbitrary-Lagrangian-Eulerian formulation (ALE) is a hybrid technique that captures the merits and minimizes the deficiencies of the Eulerian and Lagrangian descriptions. ALE formulation is commonly used for FSI simulations (Badia, Nobile, & Vergara, 2009). The term ‘arbitrary’ refers to the arbitrary mesh motion to be determined by the user or the software (Belytscho, Liu, Moran, & Elkhodary, 2014). In FSI, the boundary of the fluid mesh often follows the fluid-structure interface.

Mass conservation (continuity) and momentum balance (Navier-Stokes equation) can be expressed as:

\[ \nabla \cdot \mathbf{u}_f = 0, \]

\[ \rho_f \left[ \frac{\partial \mathbf{u}_f}{\partial t} + (\mathbf{u}_f - \mathbf{u}_g) \cdot \nabla \mathbf{u}_f \right] = \nabla \cdot \mathbf{\sigma}_f, \]

where \( \nabla = \{ \partial/\partial x, \partial/\partial y, \partial/\partial z \}^T \) is the gradient operator, \( \mathbf{u}_f \) is the fluid velocity, \( \mathbf{u}_g \) is the moving coordinate velocity, \( \rho_f \) is the fluid density, \( \mathbf{\sigma}_f = \mathbf{\tau} - \mathbf{I} \rho \) is the fluid stress, \( \mathbf{\tau} \) is the shear stress and \( \rho \) is the pressure. Furthermore,

\[ \mathbf{\tau} = \mu \left[ \nabla \mathbf{u}_f^T + (\nabla \mathbf{u}_f^T) \right], \]

where \( \mu \) is viscosity.

Although blood may exhibit non-Newtonian fluid characteristics and its viscosity can decrease with increasing the shear rate, recent works have shown that the non-Newtonian effect is significant only in very small vessels with diameter less than 0.1 mm (Ku, Elkins, & Taylor, 2005; Perktold, Kenner, Hilbert, Spork, & Florian, 1988). Hence, Newtonian flow was assumed whilst the typical properties \( \rho_f = 1050 \text{ kg/m}^3 \) and \( \mu = 0.004 \text{ Pa-s} \) were adopted here (Tang et al., 2015). As the maximum Reynolds number in the current models is 619, due to the systolic velocity 0.342 m/s and the 6.9 mm inlet diameter of Patient C, the flow could be treated as laminar.

2.3.2. Solid model

The deformation of the vessel and aneurysmal walls can readily be described by the Lagrangian description. The momentum balance equation can be expressed as:

\[ \nabla \cdot \mathbf{\sigma}_s = \rho_s \mathbf{g}_s, \]

where \( \mathbf{\sigma}_s \) is the Cauchy or, equivalently, the true stress tensor, \( \rho_s \) is solid density and \( \mathbf{g}_s \) is the local acceleration of the solid.

Because the wall of the intracranial arteries was not thick enough to be resolved in CT and MRI images, a uniform \( t_w \) (10% of the diameter (Riley, Barnes, Evans, & Burke, 1992)) was assumed here for the models before growth process. The arterial and aneurysmal walls were assumed to be a Mooney-Rivlin hyperelastic material with the following strain energy function

\[ W = c_1(I_1 - 3) + c_2(I_2 - 3) + c_3(I_1 - 3)(I_2 - 3) + c_4(I_1 - 3)^2 + c_5(I_2 - 3)^2, \]

where \( c_1 = 0.429, c_2 = -0.119, c_3 = 0.585, c_4 = 0.579 \) and \( c_5 = 0.564 \text{ MPa} \) (Valencia et al., 2015); \( I_1 \) and \( I_2 \) are the first and second strain invariants of the Cauchy-Green deformation tensor. For this nonlinear material, the elastic modulus under small strain is equal to \( 6(c_1 + c_2) \), i.e. 1.86 MPa.

2.4. Boundary conditions

2.4.1. Fluid domain

To mimic the physiological deformation of the arterial wall, a pulsatile and cyclic volume flow rate resembling the real flow conditions in patients is specified at the inlet (Ku, Giddens, Zarins, & Glagov, 1985) (Figure 3). To achieve a fully-developed flow before the aneurysm, the computation domain was extended at the inlet section by a length proportional to the specific Reynolds number using the Extrude function of SOLIDWORKS (Figure 4). Pulsatile pressure with maximum/minimum values 120/80 and 160/100 mmHg were employed at the outlet(s) (Lee et al., 2013). The former set of pressures was the normal range whilst the latter was adopted to investigate the effect of hypertension (Figure 3).
2.4.2. Solid domain

The solid domain composed of the vessel and aneurysm walls is modeled by 3D-shell elements of ADINA. The elements consider all components of stress and strain, i.e. thin shell assumptions such as zero transverse normal and shear are not adopted. The nodal parameters of the 3D-shell elements include 3 translations, 2 or 3 rotations, thickness strain and linear varying thickness strain. Mixed Interpolation of Tensorial Components (MITC) and the displacement/pressure (u/p) formulation are employed to circumvent shear and volumetric lockings, respectively (Sussman & Bathe, 2013). The latter arises when the materials are incompressible or nearly incompressible. Indeed, the adopted hyperelastic material model is incompressible. Gravity is ignored and the nodes of the shell finite elements at the inlet and outlet sections are restrained from motion. These are the common practices of FSI simulations (Bazilevs et al., 2010; Lee et al., 2013; Valencia, Ledermann, Rivera, Bravo, & Galvez, 2008).

Figure 3. Pulsatile volume flow rate at the inlet and pulsatile pressures at the outlets. Pressure waveforms with 160/100 mmHg refer to hypertension cases described in Section 3.4.

Figure 4. The meshes of fluid domains for Patient A and Patient C.
2.4.3. Conditions at the fluid-structural interface

For the computational simulations, the no-slip condition was assumed (Valencia et al., 2008). Thus, the fluid displacement $d_f$ and the solid displacement $d_s$ at the fluid-structure interface should be compatible, i.e.

$$ d_f = d_s. \quad (6) $$

Furthermore, the tractions of the two domains at the interface are in equilibrium, i.e.

$$ \sigma_f \cdot n_f + \sigma_s \cdot n_s = 0, \quad (7) $$

where $\sigma$ denotes stress, $n$ denotes the unit outward normal vector at the boundary; subscripts ‘$f$’ and ‘$s$’ represent the fluid and solid domains, respectively. At the interface, $n_f + n_s = 0$.

2.4.4. Numerical method

FSI simulations were conducted using the software ADINA 9.3.0 installed in a workstation with Intel Xeon CPU (E5-1960 v4 @ 3.20 GHz with 8 cores) and 128 GB RAM. The fluid domain was modeled by the Flow-Condition-Based-Interpolation (FCBI) 4-node tetrahedral elements. The solid domain was modeled mainly by the 4-node with a small portion of 3-node 3D-elements. ADINA provides the one-way and two-way FSI couplings. As the former does not consider the effect of structural deformation on the fluid flow, the two-way coupling mode was selected. The linearized matrix equation was solved by the direct or non-iterative solution method. A fully implicit Euler scheme with 1 ms step was used in the time stepping. The time step was chosen by balancing the computing time and the convergence with respect to the time step. For instance, the maximum effective stresses of Patient A predicted by using time steps of 2, 1 and 0.5 ms are 531.6, 495.3 and 492.7 kPa, respectively. Meanwhile, the computing times over one cardiac cycle for all models were summarized in Table 3. As the scaled models are physically larger and contain more elements, they consume more computing time than the un-scaled models. For example, the computing time of Patient A under normal pressure condition after scaling is 46.2 h while that before scaling is 39.3 h.

2.4.5. Mesh

Mesh independence tests were carried out for all models involved and results were presented in Table 2. Generally, computations were repeated for mesh grids of increasing resolution until the maximum wall effective stress remained practically unchanged when a finer mesh was employed. In the current study, meshes with 0.30 mm maximum element edge length of 0.20 mm was adopted for the model of Patient D (before and after scaling). Final meshes of the fluid domain adopted for one sidewall aneurysm (Patient A) and one bifurcation aneurysm (Patient C) before and after scaling can be seen in Figure 4. The computing time over three cardiac cycles for all models were summarized in Table 3. As the scaled models are physically larger and contain more elements, they consume more computing time than the un-scaled models. For example, the computing time of Patient A under normal pressure condition after scaling is 46.2 h while that before scaling is 39.3 h.

### Table 2. Mesh independence test.

| Models     | Maximum length of the mesh edge (mm) |
|------------|--------------------------------------|
|            | 0.35       | 0.30       | 0.25       |
| Patient A  | Before scaling | 532.8      | 495.3      | 493.8      |
|            | After scaling | 772.9      | 720.8      | 717.5      |
| Patient B  | Before scaling | 302.3      | 286.5      | 283.9      |
|            | After scaling | 659.5      | 628.1      | 622.4      |
| Patient C  | Before scaling | 478.4      | 450.5      | 446.4      |
|            | After scaling | 995.2      | 930.1      | 921.8      |

### Table 3. The computing times for all models.

| Model     | Before scaling (hour) | After scaling (hour) |
|-----------|-----------------------|----------------------|
|           | Normal pressure       | Hypertension         | Normal pressure | Hypertension |
| Patient A | 39.3                  | 40.7                 | 46.2           | 48.7         |
| Patient B | 41.6                  | 43.5                 | 47.1           | 49.1         |
| Patient C | 40.2                  | 41.4                 | 46.6           | 48.1         |
| Patient D | 42.3                  | 43.8                 | 50.1           | 50.9         |

3. Results and discussions

To assess the rupture risk of aneurysms with higher AR and smaller $t_w$ after scaling which mimics the aneurysm growth, hemodynamics parameters including flow pattern inside the aneurysm, WSS and the aneurysmal wall stress were analysed. The predictions become periodic after two cycles of blood flow and those of the third cycle would be reported.

3.1. The influence of scaling on hemodynamics

3.1.1. Flow pattern

For both sidewall aneurysms and bifurcation aneurysms, the flow patterns are not altered substantially when the models are scaled, i.e. before and after the increase in
AR and reduction of $t_w$ (Figure 5). Blood flow enters the aneurysm at the distal neck region and leaves at the proximal neck region. A vortex is observed inside the aneurysm. This flow pattern agrees well with previous studies (Liou & Li, 2008). However, there is a notable reduction in flow speed inside the aneurysm as the AR increases (Figure 5). A possible explanation is that the ratio of the neck width to the aneurysm height becomes relatively smaller as the AR increases, thereby restricting flow from entering the aneurysm. This reduction in flow speed due to an increase in AR is more dramatic in bifurcation aneurysms, as the inlet vessel would lead to an almost direct fluid impingement on the aneurysm neck. For smaller AR, the neck provides enough room for the inflow jet. For larger AR, more blood flow is diverted to the daughter vessels, effectively offering a larger obstruction to the inflow jet. Previous clinical reports have associated higher AR with a larger rupture risk (Ujiie et al., 2001), a property which cannot be explained by the flow pattern alone. A more illuminating consideration is to investigate the WSS and the wall stress which are described in the subsequent sections.

3.1.2. Wall shear stress (WSS) on aneurysmal wall

WSS is the fluid friction acting on the aneurysmal wall. For low WSS, rupture risk is aggravated and long-term damage is inflicted due to abnormal alignment of endothelial cells (Irace et al., 2004; Sho et al., 2001; Shojima et al., 2004). Instantaneous distribution of WSS at peak systole of all patient models follows an analogous pattern, with lower (higher) WSS occurring at the aneurysm (parent vessel) wall region (Figure 6), suggesting that the aneurysmal wall may be more vulnerable to long-term damage than normal vessel wall. Time averaged WSS ($TAWSS$) is a commonly used hemodynamic parameter in assessing the aneurysm rupture risk and is defined as

$$TAWSS = \frac{1}{T} \int_0^T |\tau_w| \, dt,$$

where $\tau_w$ is the WSS and $T$ represents the period of the cardiac cycle. $TAWSS$ of three control points in the aneurysmal region (namely proximal neck, distal neck and dome) for each patient-specific model were investigated.

For all the four patient-specific models, the WSS is reduced when the aneurysm attains a higher AR and a smaller $t_w$ after scaling during the whole cardiac cycle (Figure 7). Take Patient A as an example to show the results of the sidewall aneurysms. At a typical point on the proximal neck where the flow impinges, the WSS before (AR = 1.5, $t_w = 0.3$ mm) and after (AR = 1.8, $t_w = 0.15$ mm) scaling are in the range of 1 to 5 Pa and 0 to 3 Pa within a cardiac cycle whilst the $TAWSS$ are 1.94 and 1.14 Pa, respectively. Both WSS and $TAWSS$ are reduced considerably after the growth process. WSS and $TAWSS$ also decrease in the distal neck and dome regions. For instance, the $TAWSS$ at a typical point on the dome reduces from 0.21 to 0.18 Pa after growth (Table 4). For bifurcation aneurysms, similar reductions are observed. For example, the WSS for Patient C at the distal neck ranges from 0 to 2.5 Pa within a cardiac cycle, giving a $TAWSS$ of 0.97 Pa before growth. After growth, the WSS ranges from 0 to 1.6 Pa and the $TAWSS$ is 0.67 Pa. The
variation of WSS within a cardiac cycle and the TAWSS for other models can be observed in Figure 7 and Table 4 respectively.

3.2. The influence of scaling on wall stresses

As mentioned in Section 2.2, AR would increase and $t_w$ would reduce during the growth phase of the aneurysm which is mimicked by our scaling method. The influence of this scaling on the wall stresses will now be studied. Since the actual values of $t_w$ and their variations are not known, the current study focuses on the hemodynamic features and the changes in wall stresses when $t_w$ has dropped to 0.15 mm due to the growth process. Compared with the reported 0.05 mm lowest post-rupture $t_w$, (Abruzzo et al., 1998), the present 0.15 mm thickness is an intermediate thickness adopted to study the effect of scaling which leads to AR increase and wall thinning.

3.2.1. Effective stress (von Mises stress)

Predictions of solid material failures are often based on the effective stress. In recent years, it has been adopted as a criterion for predicting the aneurysm rupture risk (Volokh, 2008). The effective stress

$$\sigma_e = \sqrt{\frac{(\sigma_{xx} - \sigma_{yy})^2 + (\sigma_{xx} - \sigma_{zz})^2 + (\sigma_{yy} - \sigma_{zz})^2 + 6(\sigma_{xy}^2 + \sigma_{xz}^2 + \sigma_{yz}^2)}{2}},$$

(9)

is a scalar quantity defined using the Cauchy or true stress components $\sigma_{ij}$. In the present context, rupture may occur when the effective stress of the wall exceeds the strength of the aneurysmal wall (Isaksen et al., 2008). However, the actual strength undoubtedly varies from patient to patient. Moreover, AR often increases and $t_w$ reduces when the aneurysm grows (Suzuki & Ohara, 1978; Torii et al., 2010). Consequently, the current study focuses on how the effective stress would change as the aneurysm is scaled up in which AR increases and $t_w$ decreases.

The abrupt geometric change at the neck region always induces there the highest stress (Figure 8). On the other hand, IA ruptures often occur at the aneurysm domes. Here, both the maximum effective stresses at the neck region and the dome were captured and reported (Table 5). Furthermore, the maximum $\sigma_e$ increases for all models after scaling, suggesting that an aneurysm with a higher AR and lower $t_w$ poses a greater rupture risk. For sidewall aneurysms, the maximum $\sigma_e$ at the neck for Patient A increases from 495.3 to 720.8 kPa after scaling (AR = 1.5 & $t_w = 0.3$ mm to AR = 1.8 & $t_w = 0.15$ mm), while the corresponding trend at the dome is an increase from 60.0 to 391.4 kPa. The increase in the maximum $\sigma_e$ at the dome for Patient B due to model growth is 105 kPa (from 45.6 to 150.6 kPa), while the corresponding value at the neck is 341.6 kPa (from 286.5 to 628.1 kPa). For bifurcation aneurysms, the maximum $\sigma_e$ at the dome for Patient C increases from 55.6 to 365.0 kPa after scaling (AR = 1.2 & $t_w = 0.3$ mm to AR = 1.5 & $t_w = 0.15$ mm), while the maximum $\sigma_e$ at the neck increases from 450.5 to 930.1 kPa. The maximum $\sigma_e$ at the dome for Patient D increases by 385.9 kPa from 42.9 to 428.8 kPa, while the corresponding trend at the neck is 392.5 kPa from 315.9 to 708.4 kPa. Consequently, both sidewall and bifurcation aneurysms are
Figure 7. WSS variation over a cardiac cycle. (a) Sidewall aneurysms, (b) Bifurcation aneurysms.
Table 4. The influence of scaling on TAWSS under normal pressure condition (120 / 80 mmHg).

| Model  | AR  | Proximal neck | Distal neck | Dome |
|--------|-----|----------------|-------------|------|
| Patient A | 1.5 | 1.94           | 2.16        | 0.21 |
| Patient B | 1.9 | 0.36           | 0.91        | 0.03 |
| Patient C | 1.2 | 0.71           | 0.97        | 0.12 |
| Patient D | 2.2 | 0.49           | 0.83        | 0.09 |

| Model  | AR  | Proximal neck | Distal neck | Dome |
|--------|-----|----------------|-------------|------|
| Patient A | 1.8 | 1.14           | 1.35        | 0.18 |
| Patient B | 2.3 | 0.31           | 0.47        | 0.02 |
| Patient C | 1.5 | 0.56           | 0.67        | 0.11 |
| Patient D | 2.6 | 0.25           | 0.32        | 0.02 |

Table 5. The influence of scaling on the effective stress.

| Model  | Maximum $\sigma_e$ at aneurysmal neck (kPa) | Maximum $\sigma_e$ at aneurysmal dome (kPa) |
|--------|---------------------------------------------|---------------------------------------------|
| Patient A | 495.3                                       | 60.0                                       |
| Patient B | 286.5                                       | 45.6                                       |
| Patient C | 450.5                                       | 55.6                                       |
| Patient D | 315.9                                       | 42.9                                       |

Table 6. The influence of scaling on the first principal stress.

| Model  | Maximum $\sigma_1$ at neck (kPa) | Maximum $\sigma_1$ at dome (kPa) |
|--------|---------------------------------|---------------------------------|
| Patient A | 534.1                           | 66.3                            |
| Patient B | 305.5                           | 44.6                            |
| Patient C | 504.4                           | 59.0                            |
| Patient D | 366.2                           | 45.0                            |

Figure 8. The effective stress distribution of all models at peak systole: (a) before scaling, (b) after scaling.

Conjectured to suffer a higher risk of rupture as the aneurysm is scaled to the state with a higher AR.

3.2.2. First principal stress

Values of stress components change with the coordinate axes. The first principal stress $\sigma_1$ is the largest normal stress one can obtain by varying the directions of the coordinate axes. Similar to the effective stress, $\sigma_1$ is a commonly used stress parameter in material failure predictions. The maximum first principal stresses before and after scaling are summarized in Table 6. Their magnitudes and percentage changes due to scaling are consistent with the qualitative trend for the effective stresses presented in the last paragraph. In other words, the rupture assessments based on both the effective and first principal stresses lead to the similar outcomes.

3.3. The influence of scaling on the wall displacement

After scaling, the maximum displacements at systole for all models increase (Figure 9). Before scaling, such maximum displacements are 0.758, 0.432, 1.477 and 0.996 mm for Patients A, B, C and D, respectively. After scaling, the corresponding values are 1.403, 0.801, 1.946 and 1.478 mm, respectively. The maximum displacements for Patient A, C and D always occur at the aneurysmal dome where rupture usually occurs clinically. However, the maximum displacement for Patient B is found at the region near to but not at the dome, a variation probably due to different morphology.

3.4. The influence of hypertension

High blood pressure is believed to play an important role in the development, growth and rupture of aneurysms.
The displacement distribution of all models at peak systole: (a) before scaling, (b) after scaling.

Figure 9. The displacement distribution of all models at peak systole: (a) before scaling, (b) after scaling.

(‘Brisman, Song, & Newell, 2006; Lasheras, 2007). The current study will also investigate the effect of hypertension.

3.4.1. The influence of hypertension and AR on the wall stresses

The wall stresses for all models before and after the aneurysm growth process were studied for both normal blood pressure (120/80 mmHg) and hypertension (160/100 mmHg) conditions. The inlet volume flow rate under hypertension condition was the same as that for the normal pressure condition (Figure 3). There are majorly three reasons why we think it is a reasonable assumption. Firstly, the literature did not give a well-defined algorithm for computing the modified volumetric blood flow rate for hypertension condition (especially in the range of 160/100 mmHg which is used in the current study). And clinically it is impossible or unethical to measure changing pressure waveforms by inducing hypertension this way. Secondly, the previous papers in the literature which covered the issue of hypertension frequently used the same flow rate for both normal pressure and hypertension conditions (Lee et al., 2013; Torii et al., 2007; Torii, Oshima, Kobayashi, Takagi, & Tezduyar, 2006; Valencia & Torres, 2017). Thirdly, the current study aims to study how the wall stresses will change when the pressure condition changes from normal pressure to hypertension. The underlying assumption is that the aneurysm may rupture when its wall stress exceeds a threshold of material property. This threshold or yield stress may vary for different patients. From our computational results, the wall stresses are significantly affected by the blood pressure, but the influence of the flow rate is very small. With all these considerations, we think that using the same flow rate for both normal pressure and hypertension would still be a reasonable assumption.

The results of the maximum $\sigma_e$ and $\sigma_1$ at the dome, where the aneurysm is more vulnerable to rupture, were compared and summarized in Tables 7 and 8. Not surprisingly, the maximum wall stresses (including $\sigma_e$ and $\sigma_1$) for all models will increase as the blood pressure changes from 120/80 to 160/100 mmHg. Moreover, this increase of the wall stresses at the aneurysmal dome for the models after scaling is much more profound than those before growth with a lower AR.

Table 7. The influence of scaling and hypertension on the maximum $\sigma_e$ at the dome.

| Model  | Normal pressure | Hypertension | $\Delta\sigma_e$ |
|--------|-----------------|--------------|-----------------|
| Patient A | Before scaling  | 60.0         | 81.1            | 21.1            |
|         | After scaling   | 391.4        | 522.2           | 130.6           |
| Patient B | Before scaling  | 45.6         | 62.1            | 16.5            |
|         | After scaling   | 150.6        | 205.7           | 55.1            |
| Patient C | Before scaling  | 55.6         | 74.0            | 18.4            |
|         | After scaling   | 365.0        | 489.2           | 124.2           |
| Patient D | Before scaling  | 42.8         | 59.4            | 16.5            |
|         | After scaling   | 428.8        | 616.7           | 187.9           |

where $\Delta\sigma_e = (\sigma_e)_{\text{hypertension}} - (\sigma_e)_{\text{normal pressure}}$.

Table 8. The influence of scaling and hypertension on the maximum $\sigma_1$ at the dome.

| Model  | Normal Pressure | Hypertension | $\Delta\sigma_1$ |
|--------|-----------------|--------------|-----------------|
| Patient A | Before scaling  | 66.3         | 89.4            | 22.8            |
|         | After scaling   | 399.9        | 546.5           | 156.4           |
| Patient B | Before scaling  | 44.6         | 60.4            | 15.8            |
|         | After scaling   | 174.2        | 236.7           | 62.5            |
| Patient C | Before scaling  | 59.0         | 79.0            | 20.0            |
|         | After scaling   | 391.5        | 525.9           | 134.4           |
| Patient D | Before scaling  | 45.0         | 62.2            | 17.2            |
|         | After scaling   | 430.9        | 635.9           | 205.0           |

where $\Delta\sigma_1 = (\sigma_1)_{\text{hypertension}} - (\sigma_1)_{\text{normal pressure}}$.
For sidewall aneurysms, taking Patient A for instance, the increase of the maximum $\sigma_1$ at the dome for the model before scaling due to hypertension is 21.1 kPa, however, this increase is much larger (130.6 kPa) for the model after scaling. The maximum $\sigma_1$ at the dome for Patient A after scaling increases by 156.4 kPa due to hypertension, compared to 22.8 kPa for the model before scaling. For bifurcation aneurysms, taking Patient C for example, the maximum $\sigma_1$ at the dome for the model after scaling increases by 124.2 kPa because of hypertension, in contrast, the corresponding increase for the model before scaling is just 18.4 kPa. The increase of the maximum $\sigma_1$ for Patient C after scaling due to hypertension is 134.4 kPa, compared to only 20.0 kPa for the model before scaling. Consequently, the models with a higher AR and lower $t_w$ after scaling suffer greater rupture risk compared with the ones with a lower AR and higher $t_w$ before scaling in hypertension states.

3.5. The influence of AR increase alone

In the scaling procedure to mimic aneurysm growth, AR is increased and $t_w$ is reduced to 0.15 mm. As a control experiment, it would be instructive to examine the variation in wall stress when AR is increased but $t_w$ is kept intact at 0.3 mm.

The results show that the maximum $\sigma_1$ both at the neck and the dome increases for all the four models as the AR increases. For example, the maximum $\sigma_1$ at the neck (dome) for Patient C increases from 450.5 (55.6) to 604.7 (198.7) kPa. The results of the other models exhibit TAWSS for all models would generally decrease when the pressure is changed from a normal to a hypertension range (Table 9). The reason is that the velocity gradient would decrease due to the dilatation of the vessel and aneurysmal wall caused by hypertension. As examples, the TAWSS at the proximal (distal) neck for Patient C reduces from 0.71 (0.97) to 0.61 (0.77) Pa when the blood pressure is changed from a normal value to hypertension. The TAWSS at the proximal neck under hypertension for Patient D is 0.41 Pa, which is lower than that (0.49 Pa) under the condition of normal pressure. However, the TAWSS at the dome for all models is not sensitive to the change in pressure waveform probably due to the rather stagnant flow in the region.

Next, TAWSS under hypertension before and after scaling were studied. Results are summarized in Table 10. It is found that the TAWSS for all the models after scaling are lowered, which is similar to the situation of normal pressure. Taking the sidewall aneurysms as example, the TAWSSs of Patient B at the proximal (distal) neck is 0.35 (0.89) and 0.30 (0.47) Pa before and after scaling. The TAWSSs at the dome for the same patient before and after scaling are 0.03 and 0.02 Pa, respectively.

For bifurcation aneurysms, the TAWSSs of Patient D at the proximal (distal) neck are 0.41 (0.64) and 0.24 (0.32) Pa before and after scaling. On the other hand, the TAWSSs at the dome for the same patient are 0.09 and 0.02 Pa, respectively. Thus, aneurysms with higher AR and lower $t_w$ after scaling would experience long-term low WSS effect under the condition of hypertension, with the implication that they are at a greater risk of rupture.

3.4.2. The influence of hypertension on TAWSS

In Section 3.1.2, the influence of AR and $t_w$ on the TAWSS is studied. Based on the models before scaling, Table 9 presents the changes in TAWSS for all models due to hypertension. Our results showed that the Table 9 presents the changes in TAWSS for all models due to hypertension. Our results showed that the

### Table 9. The influence of hypertension on TAWSS before scaling.

| Model  | Proximal neck | Distal neck | Dome | Proximal neck | Distal neck | Dome |
|--------|---------------|-------------|------|---------------|-------------|------|
| Normal pressure | 1.94 | 2.16 | 0.21 | 1.88 | 2.08 | 0.21 |
| Hypertension | 0.49 | 0.83 | 0.09 | 0.41 | 0.64 | 0.09 |

### Table 10. The influence of scaling and hypertension on TAWSS.

| Model  | Proximal neck | Distal neck | Dome | Proximal neck | Distal neck | Dome |
|--------|---------------|-------------|------|---------------|-------------|------|
| Before scaling | 0.41 | 0.83 | 0.09 | 0.41 | 0.64 | 0.09 |
| After scaling | 0.61 | 0.77 | 0.12 | 0.61 | 0.77 | 0.12 |

### Table 11. The influence of scaling but keeping $t_w$ intact on the effective stress.

| Model  | Maximum $\sigma_1$ at aneurysmal neck (kPa) | Maximum $\sigma_1$ at aneurysmal dome (kPa) |
|--------|-------------------------------------------|---------------------------------------------|
| Before scaling | 495.3 | 60.0 |
| After scaling | 515.9 | 226.8 |

| Model  | Maximum $\sigma_1$ at aneurysmal neck (kPa) | Maximum $\sigma_1$ at aneurysmal dome (kPa) |
|--------|-------------------------------------------|---------------------------------------------|
| Before scaling | 286.5 | 45.6 |
| After scaling | 365.3 | 104.7 |
| Patient C | 450.5 | 55.6 |
| Patient D | 315.9 | 198.7 |
| Patient A | 495.3 | 42.9 |
| Patient B | 515.9 | 316.8 |
Figure 10. The comparison of WSS variation over one cardiac cycle between FSI and CFD. (a) Sidewall aneurysms, (b) Bifurcation aneurysms.
the same trend and are summarized in Table 11. Models with a higher AR thus suffer from higher $\sigma$, posing a higher rupture risk.

4. Conclusions

From clinical observations over the years, aneurysms with larger aspect ratios (ARs) have been associated with a higher rupture risk. The present study should be valuable in providing quantitative data and trends in constituting relations among AR increase, wall thickness ($t_w$) reduction due to aneurysm growth, hemodynamic features of the fluid medium, as well as the effective and principal stresses in the aneurysm wall. By utilizing FSI simulations on four patient-specific models before and after scaling which mimics the growth process, fluid domains with long-term low wall shear stress (WSS) effect are revealed. Moreover, the wall stresses at the aneurysm dome (the region more vulnerable to rupture) will increase notably as the AR increases and the $t_w$ reduces due to aneurysm growth. Furthermore, this phenomenon is particularly profound in hypertension condition, justifying the clinical need to avoid scenarios of high blood pressure for such patients.

Predictions from computational fluid dynamics (CFD), with the assumption of rigid walls, and fluid-structure interaction (FSI) on patient-specific models have been compared. The flow patterns between the two approaches are very similar while the fluid shear stresses obtained from FSI are smaller than those from CFD simulations due to the dilation of the aneurysm (Figure 10). For example, the TAWSS at the proximal neck for Patient A, B, C and D before scaling based on CFD are 2.15, 0.42, 0.78 and 0.57 Pa, while the corresponding values based on FSI are 1.94, 0.36, 0.71 and 0.49 Pa, respectively. Besides, the FSI could provide the response of the solid domain for the coupled system, which could not be obtained by CFD alone. Advantages of the FSI scheme are thus illustrated.

The merits of performing FSI include its non-invasive nature and relatively low cost. However, there are some limitations in the current study. Firstly, blood is modeled as a Newtonian fluid, and non-Newtonian models should be incorporated in the future to account for the shear thinning behavior. Secondly, the thickness of the aneurysm sac and the vessel walls is assumed to be uniform, arising from the limitation in the resolution of available imaging technology at our clinical centers. Despite these limitations, current effort should be valuable in providing quantitative data and trends in constituting relations between aneurysm growth and its rupture risk. In the future, further patient studies will be collected to provide more substantive data sets.

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