Journal of Biomechanics 47 (2014) 3695–3703

Contents lists available at ScienceDirect

Journal of Biomechanics

journal homepage: www.elsevier.com/locate/jbiomech
www.JBiomech.com

Realistic non-Newtonian viscosity modelling highlights hemodynamic differences between intracranial aneurysms with and without surface blebs[☆]

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ARTICLE INFO

Article history:
Accepted 25 September 2014

Keywords:
Newtonian
Non-Newtonian fluid
Intracranial aneurysms
Blebs
Wall shear stress

ABSTRACT

Most computational fluid dynamic (CFD) simulations of aneurysm hemodynamics assume constant (Newtonian) viscosity, even though blood demonstrates shear-thinning (non-Newtonian) behavior. We sought to evaluate the effect of this simplifying assumption on hemodynamic forces within cerebral aneurysms, especially in regions of low wall shear stress, which are associated with rupture. CFD analysis was performed for both viscosity models using 3D rotational angiography volumes obtained for 26 sidewall aneurysms (12 with blebs, 12 ruptured), and parametric models incorporating blebs at different locations (inflow/outflow zone). Mean and lowest 5% values of time averaged wall shear stress (TAWSS) computed over the dome were compared using Wilcoxon rank-sum test. Newtonian modeling not only resulted in higher aneurysmal TAWSS, specifically in areas of low flow and blebs, but also showed no difference between aneurysms with or without blebs. In contrast, for non-Newtonian analysis, bleb-bearing aneurysms showed significantly lower 5% TAWSS compared to those without ($p=0.005$), despite no significant difference in mean dome TAWSS ($p=0.32$). Non-Newtonian modeling also accentuated the differences in dome TAWSS between ruptured and unruptured aneurysms ($p<0.001$). Parametric models further confirmed that realistic non-Newtonian viscosity resulted in lower bleb TAWSS and higher focal viscosity, especially when located in the outflow zone. The results show that adopting shear-thinning non-Newtonian blood viscosity in CFD simulations of intracranial aneurysms uncovered hemodynamic differences induced by bleb presence on aneurysmal surfaces, and significantly improved discriminant statistics used in risk stratification. These findings underline the possible implications of using a realistic model of blood viscosity in predictive computational hemodynamics.

1. Introduction

The detection of incidental, asymptomatic, unruptured aneurysms places onus on involved clinicians to make recommendations with respect to treatment versus observation, balancing the relative low risk of rupture against the risk of complications with treatment (Investigators, 1998; Wiebers, 2003). To this end, research has tried to identify clinical (Investigators, 1998; Wiebers, 2003), morphological (Dhar et al., 2008; Ma et al., 2004), and hemodynamic (Cebral et al., 2005b; Shojima et al., 2004) aneurysm characteristics which may be associated with an increased risk of rupture, and may assist in the treatment decision.

Hemodynamic forces, such as the wall shear stress (WSS), have been shown to impact arterial wall mechanics and play a role in the pathogenesis of aneurysm growth and rupture (Sforza et al., 2009). Consequently, recent studies have focused on the hemodynamic environment of aneurysmal arteries (Cebral et al., 2011; Lauric et al., 2013; Valen-Sendstad et al., 2013; Xiang et al., 2011). Computational fluid dynamic (CFD) simulations often involve simplified assumptions of blood properties by adopting a Newtonian fluid model which assumes constant fluid viscosity regardless of the change in shear rate (Xiang et al., 2012). However, blood is a shear-thinning fluid characterized by lower viscosity at increased flow and by high viscosity in regions of reduced shear

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Abbreviations: CFD, Computational Fluid Dynamics; Non-Newtonian CV, non-Newtonian with constant velocity boundary condition; Non-Newtonian CWSS, non-Newtonian with constant wall shear stress boundary condition; TAWSS, Time Averaged Wall Shear Stress; WSS, Wall Shear Stress; 5% LTAWSS, TAWSS on the 5% dome area covered by lowest TAWSS; 5% HTAWSS, TAWSS on the 5% dome area covered by highest TAWSS

[☆] IRB approval: This research was approved by Tufts Health Sciences Campus Institutional Review Board.

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http://dx.doi.org/10.1016/j.jbiomech.2014.09.027
0021-9290/

rate, which are often characteristic to aneurysms and aneurysmal blebs (Schirmer and Malek, 2007b). These rheological properties are ignored by Newtonian representations and are better modeled employing non-Newtonian blood viscosity models, which show hematocrit dependence. Thus, questions remain if assuming constant blood viscosity provides a reasonable approximation of flow in regions of low shear stress, which characterizes aneurysmal geometries. Recent studies reported strong correlation between Newtonian and non-Newtonian viscosity models for most aneurysms (Castro et al., 2013; Cebral et al., 2005a; Evju et al., 2013; Xiang et al., 2012), although some disagreement was suggested for aneurysms with complex shapes (Xiang et al., 2012).

Size and shape characteristics of aneurysms have been previously analyzed in association with rupture risk (Baharoglu et al., 2012). Ruptured aneurysms tend to be larger and have more irregular shapes compared to their unruptured counterparts. They are often characterized by lower overall WSS, as well as larger percentage area covered by low WSS (Lauric et al., 2013; Lu et al., 2011). In addition, ruptured aneurysms tend to present with blebs, which often co-localize with the site of rupture (Beck et al., 2003). Blebs are regions of slow flow, characterized by lower WSS compared to the surface of their host aneurysms (Shojima et al., 2004). Moreover, ruptured blebs have been shown to have significantly lower WSS compared to unruptured blebs (Kawaguchi et al., 2012). Consequently, the hemodynamic evaluation of aneurysmal blebs is a critical aspect of rupture risk stratification.

This study investigates the effect of employing the simplified assumption of constant viscosity on hemodynamic forces within cerebral aneurysms, particularly in the case of bleb-bearing aneurysms. Previous research comparing Newtonian and non-Newtonian viscosity models have been limited by the small number of aneurysms which did not allow for statistical comparison. The aim of this study is to quantify the implications of assuming constant blood viscosity on discriminant statistics used in aneurysm risk stratification.

2. Materials and methods

2.1. Patient-derived models

Consecutive high-resolution 3D rotational angiography (3DRA) datasets of patients with intradural aneurysms were examined for this study. The aneurysm location was restricted to aneurysms originating off the internal carotid artery. Consequently, 26 aneurysms (12 ruptured) were available for analysis. Out of the 26 aneurysms, 12 aneurysms (8 ruptured) were classified as having blebs by the treating neurosurgeon. All angiographic imaging within the ruptured set were obtained in urgent fashion and prior to vasospasm onset.

2.2. Cerebral angiography and data processing

Three-dimensional cerebral angiograms were obtained under general anesthesia from either Philips Integris (Bothell, WA) or Siemens Artis (Malvern, PA) biplane systems, and reconstructed using their respective clinical software packages, to yield a 3D volume (Fig. 1A). Volumetric data sets, including aneurysm and parent vessel, were analyzed in Amira version 5.4 (FEI Visualization Sciences Group, Burlington, MA) for segmentation in 3D space (Fig. 1A).

2.3. Patient-derived models

The segmented surfaces were used to create polyhedral meshes of approximately 250,000–600,000 cells with a boundary layer enhancement. Grid independence was established prior to the beginning of the study by performing meshing of selected models at increasing mesh resolution. The final mesh was created using Star-CCM+(CD-Adapco, Melville, NY). The ICA segment proximal to the site of the aneurysm was kept sufficiently long (at least several times the diameter of the parent vessel) in order to enable the laminar flow to become fully developed and avoid entrance effects.

2.4. Parametric models

Synthetic models of carotid ophthalmic aneurysms were constructed using SolidWorks (Concord, MA). An initial aneurysm was modeled as a sphere with radius 4 mm as previously described (Lauric et al., 2013). Two additional models were created by adding a bleb modeled as a hemisphere with a radius of 1 mm to the aneurysm surface, located in the inflow zone (45°) and in the outflow zone (135°), respectively, in a plane perpendicular to the neck plane (Fig. 1C).

2.5. Bleb removal analysis

Blebs were digitally removed from patient-derived models by local Laplacian smoothing followed by aneurysm surface reconstruction in MeshLab version 1.3.1 (ISTI-CNR, Pisa, Italy). Hemodynamic analysis was performed before and after bleb removal.

2.6. Computational fluid dynamic modeling

For both patient and parametric models computational fluid dynamics (CFD) simulations were performed using Ansys Fluent 14.0 (Ansys, Lebanon, NH) assuming two different viscosity models.

First, a Newtonian model was applied with constant viscosity of 0.0035 kg/(m s) and density of 1070 kg/m^3. The velocity magnitude was scaled to guarantee an ideal parent vessel WSS of approximately 1.5 Pa in the proximity of the aneurysm (Malek et al., 1999) (Fig. 1B).

Second, a non-Newtonian model, which is a more realistic representation of blood viscosity behavior, was applied using the Carreau viscosity model (Schirmer and Malek, 2007a, 2007b) with a density of 1070 kg/m^3 (details available as Supplementary material). The velocity magnitude was rescaled in order to maintain the ideal WSS of 1.5 Pa on the parent vessel. This model is referred to as non-Newtonian with constant WSS boundary condition (non-Newtonian CWSS). The justification for this model stems from the hypothesis that the arterial tree follows the principle of minimum energy expenditure described by Murray's Law and validated in the cerebral circulation by Rossitti and Lofgren (1993), mediated by an underlying endothelial regulatory mechanotransduction process aimed at maintaining WSS constant on the arterial side (LaBarbera, 1990; Langille and O'Donnell, 1986; Murray, 1926).

Third, to account for any differences arising from rescaling of the velocity magnitude between the Newtonian and non-Newtonian model, the non-Newtonian model described above was reapplied, this time using the same velocity magnitude as derived for the Newtonian model. This model is referred to as non-Newtonian with constant velocity boundary condition (non-Newtonian CV).

Regardless of the viscosity model used, the scaled pulsatile flow was applied normal to the inlet for three complete cardiac cycles to allow the flow to fully develop and the third cycle was used for analysis (Ford et al., 2005). Each cycle period was $T=1$ s and had a time step of $t=0.005$ s with the peak-systole at $t=0.16$ s. At the outlets, gauge pressure was set to zero Pascal.

All post-processing analysis was performed using EnSight 10.0 (Computational Engineering International, Apex, NC). For each model, the aneurysm dome was separated from the parent vessel and WSS statistics were evaluated on the dome (Fig. 1B). For both parametric and patient-derived models, the time averaged WSS (TAWSS) was evaluated over the aneurysm surface. The spatial mean was computed using an area weighted summation over the aneurysmal surface for TAWSS (Lauric et al., 2013). Additional analysis was focused on the aneurysmal area covering the lowest and the highest TAWSS distribution range, as both low and high WSS were previously associated with aneurysm growth and rupture (Meng et al., 2013). Similar to Lauric et al. (2013), statistics were evaluated on the 5% dome area of lowest TAWSS (5% LTAWSS), identified on the aneurysm dome using custom processing software code (Matlab version 7.10, MathWorks, Natick, MA). The 5% dome area of highest TAWSS (5% HTAWSS) was also evaluated.

2.7. Statistical analysis

JMP statistical software (version 9.0.2, SAS Institute, Cary, NC) was used to evaluate the performance of all parameters in discriminating between aneurysms with and without blebs. Statistical significance was assumed for $p<0.05$. All variables were tested independently using the student *t*-test analysis for normally distributed data, and Wilcoxon rank-sum test for non-normally distributed data. Bivariate analysis was used to quantify statistical correlation, as described by the square of the correlation coefficient (R^2).

3. Results

3.1. Demographics and presentation

A total of 26 sidewall aneurysms from 26 patients (59 ± 12.10 years) were available for analysis. 12 aneurysms (61.58 ± 11.55 years)