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Simulation of a pulsatile non-Newtonian flow past a stenosed 2D artery with atherosclerosis

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ABSTRACT

Atherosclerotic plaque can cause severe stenosis in the artery lumen. Blood flow through a substantially narrowed artery may have different flow characteristics and produce different forces acting on the plaque surface and artery wall. The disturbed flow and force fields in the lumen may have serious implications on vascular endothelial cells, smooth muscle cells, and circulating blood cells. In this work a simplified model is used to simulate a pulsatile non-Newtonian blood flow past a stenosed artery caused by atherosclerotic plaques of different severity. The focus is on a systematic parameter study of the effects of plaque size/geometry, flow Reynolds number, shear-rate dependent viscosity and flow pulsatility on the fluid wall shear stress and its gradient, fluid wall normal stress, and flow shear rate. The computational results obtained from this idealized model may shed light on the flow and force characteristics of more realistic blood flow through an atherosclerotic vessel.

1. Introduction

Atherosclerosis is the main cause of heart attack and stroke, particularly in western developed countries. This disease causes a gradual stenosis of the lumen and hardening of the artery wall because of accumulation of lipids (e.g., low density lipoproteins or LDL) in the intima. The progressive build-up of deposits in the arterial wall may form a plaque that protrudes into the lumen and restricts the blood flow. In some cases a mature plaque may rupture suddenly without early warning and the broken plaque debris may block smaller arteries downstream. If the carotid artery (which supplies blood to the brain) is affected, one may suffer from stroke; if the coronary artery (which supplies blood to the heart) is affected, one may suffer from a heart attack. Currently the mechanism of plaque rupture is not clear despite a substantial amount of research [29]. Because the atherosclerotic plaque may project into the lumen from the wall, the blood flow in the lumen changes essentially from flow through a straight pipe to flow past an irregular obstacle. There are also corresponding changes in the forces (shear and normal stresses) exerted by the flowing blood on the plaque surface. These altered forces may play an important role in the formation of fatty streaks or even in the rupture of more advanced lesions. Moreover, the altered flow and forces may directly affect the vascular endothelial cells lining the inner-most artery wall, or indirectly influence the vascular smooth muscle cells (SMCs) comprising the media.

The low wall shear stress (WSS) hypothesis was advocated by C.G. Caro et al. [5,6] in a series of papers and is a currently accepted theory for atherogenesis: low endothelial shear stress may decrease the secretion of arterial relaxing factor nitric oxide (NO) [7], promote inflammation through the secretion of chemoattractants [15] and increase endothelial permeability [21]. Generally, atherosclerotic lesions are observed in blood vessels that are bifurcated or highly curved.

While the most popular theory to explain atherogenesis is the low WSS theory (low wall shear stress initiates plaque build-up), competing theories suggest that other characteristics of the flow such as shear rate (SR) may be important [22]. Experiments by [39] on human umbilical vein monolayers show that endothelial cells migrate away from regions with high wall shear stress gradients (WSSGs) and have increased proliferation rates. This kind of behavior could drastically impact the permeability of the endothelium, enhance the transport of LDL into intima and initiate

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plaque precursors. Forces exerted by the flowing blood on the endothelium may be decomposed into two perpendicular components: the component tangential to the endothelium (WSS), and the component normal to the endothelium (wall normal stress, or WNS). An increased WNS could impact plaque formation in several ways. First, increased WNS may stretch vascular SMCs residing in the media and Thubrikar [41] has shown that non-uniform stretching of SMCs could lead to vascular disease. Second, increased WNS means increased blood pressure (hypertension) which is a risk factor for strokes and heart attacks. Finally, higher WNS on the arterial wall may facilitate the deposition of LDL into the intima [4]. It is possible that high concentrations of LDL could lead to more oxidized LDL which could lead to plaque formation [16]. The combination of higher WNS and lower WSS (which could increase endothelial permeability) may produce additional synergistic effects.

There already exist many experimental and computational works that try to evaluate the fluid WSS on the plaque surface. Steinman et al. [35] investigated how stenotic geometry affects flow patterns by employing both concentric and eccentric carotid bifurcation models, assuming the same stenotic severity. Kohler et al. [24] investigated the WSS by using magnetic resonance imaging (MRI) measurements of the velocity field and comparing them with simulation results. Glickman et al. [2] conducted *in vitro* laboratory experiments of non-pulsatile flows through atherosclerotic carotid bifurcations. August et al. [1] examined the WSS in the carotid artery by computation and laboratory measurements. Teng et al. [40] studied critical flow shear stress and its association with plaque rupture using both *in silico*3D models and *in vivo* MRI data. Stroud et al. [37] used modeling and simulation to study a 2D plaque model while Fischer et al. [17] introduced a new numerical method for the computational study of arterial blood flow with weak turbulence. Tan et al. [38] predicted the flow patterns in a carotid artery with atherosclerosis by using transitional variants and a two-equation model of turbulence. Grinberg et al. [20] investigated transient turbulence in a bifurcated carotid artery (built from MRI data) through high resolution simulations in three dimensions. Wong et al. [43] and Poepping et al. [32] performed *in vitro* studies on turbulence intensity in the downstream region of an arterial plaque. Chen et al. [8,10] studied the relationships between force/flow and the intimal hyperplasia (IH) in stented coronary arteries by computational and experimental approaches. All of these studies investigated the flow field (laminar or turbulent) and force field (mostly WSS) of blood flow past a stenosed 2D or 3D rigid artery (either obtained from MRI or idealized).

In this paper, we perform detailed numerical simulations of pulsatile/non-pulsatile and Newtonian/non-Newtonian blood flow past a localized stenosis in an idealized 2D blood vessel. It appears that there are generally fewer studies that address fluid WNS and flow SR associated with an atherosclerotic plaque. Therefore we include these two quantities in our studies in addition to the usual metrics of atherogenesis, WSS and WSSG. The goal is to perform a systematic parameter study to understand how flow profile, vessel geometry and plaque size affect WSS, WSSG, WNS and SR. To the best of our knowledge, such a systematic study is absent from the literature.

We would like to emphasize that similar to many existing studies, our work is based on the assumption that the artery is rigid and the flow is laminar. We do not use realistic vessel geometry from an actual patient (which may be obtained via MRI or ultrasound, as discussed above). Instead, we assume our domain to be a generic stenosed arterial segment which is compromised by atherosclerotic plaques of different severity. Our results may provide insight into the case of unsteady, high Reynolds number flow in a diseased artery and the associated force fields. While the geometry of our problem is idealized, it nevertheless serves as a platform to study wall stresses in arteries with few branches, and potentially as a way to study the absorption of LDL and other macromolecules; for example Olgac et al. [31] use a similar idealized vessel geometry.

The remainder of the article is structured as follows: in Section 2 the mathematical formulation of the model problem of blood flow past a stenosed artery is given and the corresponding numerical method is briefly described. In Section 3 verification and validation of the simulation results are made. In Sections 4, 5 and 6 the major simulation results are presented and discussed. In Section 7 a summary and a discussion of our work are given.

2. Mathematical formulation and numerical method

Blood flow through a stenosed arterial segment with atherosclerosis can be modeled by an incompressible, viscous fluid with a viscosity that could be shear-rate dependent. We simulate the fluid through a 2D flow tunnel (with width $2a$ and length $25a$) with a stenosis taking the form $y=-a+A\exp[-(x-x_0)^2/b^2]$, where parameters A and b control the stenosis height and width, respectively, and x_0 is the center of the stenosis. Fig. 1 shows the geometry of the model problem with seven different stenoses to represent plaques of different size and shape. A velocity profile $U(y,\ t)$ is given at the inlet (left boundary) to model the pulsatile flow.

The fluid dynamics is governed by the incompressible Navier–Stokes equations,

$$\rho\left(\frac{\partial \mathbf{u}}{\partial t}+\mathbf{u}\cdot\nabla\mathbf{u}\right)=-\nabla p+\nabla\cdot\mathbf{S}, \tag{1}$$

$$\nabla\cdot\mathbf{u}=0, \tag{2}$$

where ρ is the density, p is the pressure, $\mathbf{u}$ is the velocity, and $\mathbf{S}=2\eta\mathbf{D}$ with $\mathbf{D}=(\nabla\mathbf{u}+\nabla\mathbf{u}^T)/2$. For a Newtonian fluid, $\eta/\rho=\nu$, and the Reynolds number is defined by $Re=a\overline{U}/\nu$ with $\overline{U}$ being the averaged incoming velocity. For a non-Newtonian fluid, the viscosity is shear rate dependent $\eta=\eta(\dot\gamma)$. In our work the Carreau–Yasuda model [18,19] is used where the viscosity of the blood is described by

$$\eta=\eta_\infty+(\eta_0-\eta_\infty)[1+(\lambda\dot\gamma)^{a_0}]^{(n-1)/a_0}, \tag{3}$$

where $\dot\gamma$ is the flow shear rate which is defined by $\dot\gamma=\sqrt{2D_{ij}D_{ij}}$ with $D_{ij}=(u_{i,j}+u_{j,i})/2$. The Reynolds number for the non-Newtonian fluid can be defined as $Re=\rho a\overline{U}/\eta(0)$. The Navier–Stokes equations together with the Carreau–Yasuda model have been used for modeling and simulation of blood flows in the literature and very good agreements between computational results and laboratory measurements have been found [18,19,12–14].

A fractional-step velocity correction method [25] is used to solve Eqs. (1) and (2). The discretized form can be obtained by splitting Eq. (1) into two substeps as,

$$\hat{\mathbf{u}}=\mathbf{u}^n+\Delta t(\eta\nabla^2\mathbf{u}^n/\rho+\nabla\eta\cdot(\nabla\mathbf{u}^n+(\nabla\mathbf{u}^n)^T)/\rho-\mathbf{u}^n\cdot\nabla\mathbf{u}^n), \tag{4}$$

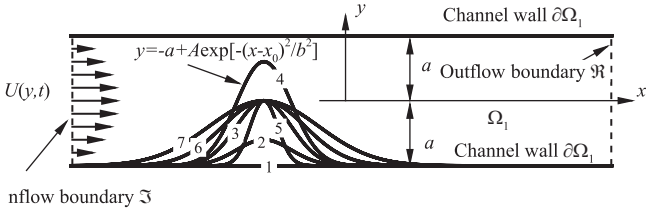

Fig. 1. Schematic representation of a 2D stenosed artery. The geometrical parameters are: (1) $A/a=0$ (channel flow), (2) $A/a=0.4$ and $b/a=1.0$, (3) $A/a=1.0$ and $b/a=1.0$, (4) $A/a=1.6$ and $b/a=1.0$, (5) $A/a=1.0$ and $b/a=0.5$, (6) $A/a=1.0$ and $b/a=1.5$, and (7) $A/a=1.0$ and $b/a=2.0$.