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Low density lipoprotein transport through patient-specific thoracic arterial wall

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ABSTRACT

Background and aims: The distribution of Low density lipoprotein (LDL) within the arterial wall is helpful in understanding the onset and development of atherosclerosis. The objective of the study is to study the transport and LDL distribution within patient-specific arterial wall using computational analysis under normal and hypertensive conditions.
Methods: Patient specific model of the thoracic aorta is computationally examined. The arterial wall is treated macroscopically as homogeneous (one layered) porous media of variable thickness. The interfacial lumen-arterial wall (endothelium) coupling is achieved by the Kedem-Katchalsky equation.
Results: High values of LDL are located at areas where WSS values range from 0.4 N/m^2 to 1.5 N/m^2 for normal conditions. In this case the Pearson correlation coefficient r between LDL values and WSS is equal to −0.655 denoting a strong negative linear correlation. In the case that hypertension takes place, high LDL values are located at areas where WSS values range from 0.59 N/m^2 to 1.7 N/m^2 and the corresponding Pearson correlation coefficient r is equal to −0.808 denoting a very strong negative linear correlation. For the same parabolic intake flow velocity profile, the luminal surface concentration of LDL is 0.2–2.1% higher than that of the bulk flow for the normal pressure and 0.4–3.4% higher than that of the bulk flow for the hypertensive pressure. For normal conditions, the concentration of LDL at the endothelium/media interface is considerably lower (almost 20 times) than the LDL concentration value at lumen/endothelium interface. For hypertensive conditions, the LDL concentration at the endothelium/media interface is only 4.5 times lower than the corresponding luminal (endothelium side) concentration. The lumen/endothelium side locations (mainly the concave parts) of low WSS - high LDL concentration values coincide with those of high wall-side LDL concentration.
Conclusions: The transport and LDL distribution is affected by elevated transmural pressure which causes higher LDL concentration. Thus, hypertensive conditions theoretically enhance atherosclerosis.

1. Introduction

In every year up until now, since 1900, except in 1918, cardiovascular disease accounted for more deaths than any other major cause of death in the United States. Specifically, more than 2150 Americans die of cardiovascular disease each day, which is an average of one death every 40 s [19]. Several studies have demonstrated that a major cause of cardiovascular disease is atherosclerosis. At the same time the accumulation of Low Density Lipoprotein (LDL) macromolecules within the arterial wall is a well-established contributor to atherosclerosis progression. This undeniable fact forces us to numerically investigate the mechanism (the mass transport from lumen to arterial wall) through which this disease tends to grow.

The mass transport within the arterial wall is a highly complex physical phenomenon depending upon biological, chemical and mechanical factors [6]. Since the blood flow pattern in the aorta is intricate and the measurement of blood flow in vivo as well as in vitro is a difficult task, the numerical flow simulation is the reliable tool through which we can obtain detailed insight into the hemodynamic factors that are responsible for the process of atherosclerosis. So far, various numerical studies have been performed based on idealised arteries [1,14,24,36]; and on realistic arteries [13,17,18,22,26]. However, the assumption

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Nomenclature

C	concentration (gr/l)
D	diffusivity (m^2/s)
D′	diffusivity per unit length (m/s)
Δp	pressure drop (N/m^2)
J	flux (m/s)
K	permeability (m^2)
K′	solute lag
L	hydraulic conductivity (m^2 s/gr)
L″	thickness (m)
R	radial location from the centerline (m)
p	pressure (N/m^2)
r	constant consumption rate
u	velocity (m/s)

Subscripts

l	lumen
lag	coefficient
o	inlet
p	plasma
s	solute
v	volume
eff	effective property
w	wall

Superscripts

end	endothelium
m	media

Greek symbols

μ	molecular viscosity (Pa s)
σ_d	osmotic reflection coefficient of the endothelium
σ_f	solvent reflection coefficient
ρ	density (Kg/m^3)
ε	porosity

made in the first category automatically implies that the simplification of simulating an idealize artery can lead to an underestimation of the influence of the geometry such as the concave parts of an artery, which in turn does not provide satisfactory estimations of the flow pattern and the LDL distribution at the lumen/endothelium interface as well as inside to the arterial wall resulting in substantial errors. The majority of studies based on realistic arteries have emphasized the effect of wall shear stress (WSS) on the lumen side concentration of LDL in the aortic arch or the ascending aorta as the atherosclerotic plaques tend to preferentially grow up in these areas. Any perturbation of flow in the region close to endothelium interface, resulting from a complex geometry configuration and flow oscillation, initiates mass flow disturbance to the endothelium and subsequently to the arterial wall.

In the last two decades, the computational analysis of macromolecules transport has been approached via either wall-free, lumen-wall or multi-layer modeling [24]. Wall-free modeling is the simplest approach analysis since it is restricted within the lumen and the transport of LDL to the wall is treated as a simple boundary condition. The lumen-wall approach considers flow - mass transport within the artery wall and the wall is considered to be a single homogeneous layer. However the most appropriate approach nowadays is the multi-layer model [2,3,7,9,13,31,36].

This research aims to quantifiably define LDL concentration within patient-specific arterial wall model. A normal realistic human thoracic aorta is computationally examined and the arterial wall is treated as macroscopically homogeneous porous media of variable thickness. Both the fundamental flow-mass transport equations in the lumen as well as the equations within the patient-specific arterial wall are simulated under steady state flow conditions. The hypertension effect on the flow pattern, the luminal (endothelium side) concentration of LDL and the LDL distribution inside the arterial wall are also discussed.

2. Methods

2.1. Acquisition of anatomy data

The patient specific model of the thoracic aorta was reconstructed from computed tomography (CT) images using an image segmentation tool, software Materialize Mimics Version 10.01. The reconstruction of the wall thickness was a difficult task to be performed. Axial CT images (DICOM files) were segmented in cross-sections perpendicular to the luminal centreline and the luminal and vascular wall surfaces were semi-manually defined. Using the delineated cross-sectional contours, the luminal surface and the vascular wall surfaces were constructed with cubic B-splines. Typical reconstruction of the 3D thoracic artery geometry is shown in Fig. 1A. The length of the acquired thoracic aorta is 13.0 cm; the lumen average diameter is 3.0 cm and the average wall thickness 4.0 mm. Fig. 1B shows the computational grids for the lumen and arterial wall. A mesh sensitive study was performed to solve the fundamental flow-mass transport equations in the lumen, Fig. 1C and D. The final grid size was comprised of 758365 nodes, 536304 cells and 1830213 faces for the lumen's grid and 356751 nodes, 258000 cells and 873079 faces for the media's grid. Numerical experimentation has shown that nearly 300000 grid nodes (hexahedral cell formation) and 2000000 grid nodes (tetrahedral cell formation) are needed to reach grid–independent (WSS) and LDL values [5].

2.2. Flow and mass transport equations

The applied numerical code solves the governing 3D, steady Navier-Stokes equations for lumen flow and the mass transport equation (LDL) for the arterial lumen. The arteries are treated as being of non-elastic material. All computational grid data as well as all physical flow data determined from the boundary conditions were imported into the main computational fluid dynamics (CFD) solver. The patient specific arterial wall is considered as permeable media. The Navier-Stokes equations and Darcy's Law have been applied for lumen flow analysis and arterial wall flow, respectively [29]. The LDL transport in the fluid domain has been calculated using convection-diffusion equation. The convection-diffusion-reaction equation [29] has been calculated through the arterial wall.

2.3. Flow equations

Lumen flow: The mass flow equation for the lumen is,

$$\nabla\cdot\vec{u}_l = 0 \tag{1}$$

$\vec{u}_l$ (m/s) is the lumen velocity vector. The conservation of momentum is,

$$\nabla\cdot(\rho\vec{u}_l\vec{u}_l) + \nabla p_l = \nabla\cdot(\bar{\tau}) \tag{2}$$

p_l (N/m^2) is the blood static pressure within lumen; $\bar{\tau}$ (N/m^2) the shear stress tensor and $\rho\vec{g}$ (N/m^3) the gravitational body force. The shear stress tensor $\bar{\tau}$ is,

$$\vec{\tau} = \mu_l\left[\nabla\vec{u}_l + \nabla\vec{u}_l^{\,T}\right] - \frac{2}{3}\nabla\cdot\vec{u}_l I \tag{3}$$