ORIGINAL ARTICLE

Oscillating LDL accumulation in normal human aortic arch - shear dependent endothelium

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Abstract
Objective: Abnormal mass transfer of blood components to the arterial walls initiates atherosclerosis. Understating the role of mass transfer within the arterial walls requires quantitative analysis. The oscillating lipid accumulation in the aortic wall is examined in the normal human aortic arch with shear dependent endothelium properties.
Methods: A semi-permeable nature of the arterial wall computational model, applied in the normal human aortic arch under unsteady normal flow and mass conditions, is incorporated with hydraulic conductivity and permeability treated as wall shear stress dependent. The coupling of fluid dynamics and solute dynamics at the endothelium was achieved by the Kedem-Katchalsky equation. A typical aortic arch blood flow waveform at resting conditions and lasting 800 msec is applied.
Results: With constant values of water infiltration and endothelial permeability the surface vertex average normalized luminal concentration is 4.25 % higher than that at the entrance. With shear dependent values the surface vertex average normalized luminal concentration is 7.3 % higher than at the entrance. The luminal surface concentration at the arterial wall is flow-dependent with local variations due to geometric features. Concave sides of the aortic arch exhibit, relatively to the convex ones, elevated low density lipoprotein at all time steps.
Conclusions: The degree of elevation in luminal surface LDL concentration is mostly affected from the water infiltration velocity at the vessel wall. Shear dependent endothelial values must be taken into account whenever fluid and mass flow within the arterial system is incorporated. Hippokratia 2011; 15 (1): 22-25

Key Words: oscillating LDL transport, shear dependent endothelium, aortic arch

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Abnormal mass transfer of blood components to the arterial walls initiates atherosclerosis. Understating the role of mass transfer within the arterial walls requires quantitative analysis. Regional variations in the permeability of arterial endothelium may contribute to the localization of atherosclerosis[1]. Lipids and inflammatory cells infiltrate into the artery wall eventually forming plaques and subsequently artery stenosis. Wall Shear Stress (WSS)-induced biological responses of endothelial cells and transmural filtration flow play important roles in localized Low Density Lipoprotein (LDL) accumulation in vascular walls[2]. The effects of local WSS on the endothelial cell layer were numerically analyzed in a coupled blood-wall mass transport of LDL model[3] observing high luminal surface LDL concentrations in low WSS regions. An increased permeability to LDL, as it is the case of increased plasma LDL concentration, increases atherosclerosis[4]. In vitro tests have shown that vascular permeability is acutely sensitive to WSS[5]. A fluid-wall model with shear-dependent transport parameters was used to investigate the LDL transport in a human right coronary artery[6]. Higher permeability of the endothelium caused excessive influx of LDL to the subendothelial layer.

In the current research work a homogeneous and semi-permeable nature of the arterial wall computational model using non-Newtonian blood flow is incorporated to study oscillating mass transport patterns in normal human aortic arch using shear dependent endothelial properties namely hydraulic conductivity and endothelial permeability.

Methods

Firstly, the aortic arch centerline is generated. Thereafter, the daughter vessels centerlines are generated and placed at the appropriate aortic arch centerline locations. Various vessel cross-sections, taken every 1.0 mm, are set perpendicular to ascending-descending aortic arch and daughter vessel centerlines at appropriate locations. The grid size was comprised of 796647 cells, 1876198 faces and 317914 nodes, Figure 1. The numerical code solves the governing Navier-Stokes flow equations and the mass transport of LDL equation. The assumptions made about the nature of the blood flow are, 3D, unsteady, laminar and isothermal. The arterial wall is comprised from homogeneous, non-elastic and permeable material[7]. We assume the molecular diffusivity to be isotropic[8] (=50.0x10^{-12} m^2/

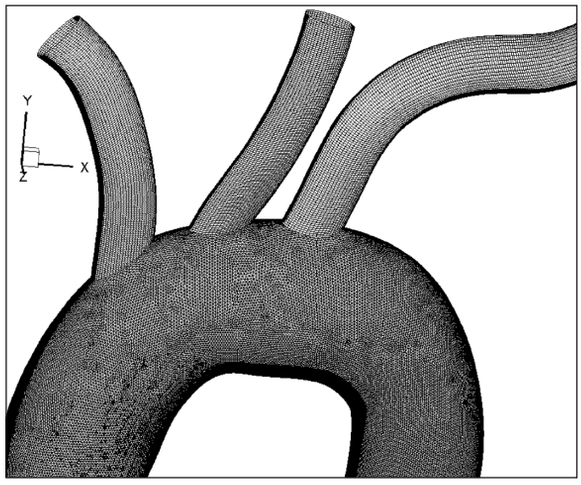

Figure 1: Computational grid details of the human aortic arch. The tested grid is comprised from 317914 nodes.

s). The coupling of fluid dynamics and solute dynamics at the endothelium was achieved by the Kedem-Katchalsky[9] equation. The shear dependent water infiltration velocity V_w (m/s) is calculated[10-12],

$$V_w(\tau_w=[0.392x10^{-12} \ln(|\tau_w|+0.015) + 2.7931\chi10^{-12}] \ 5933.33$$
(Equation 1)

Low WSS (N/m^2) or τ_w results into decreased V_w and vice versa. For the shear dependent endothelial permeability coefficient K the following equation is used[12],

$$K(C_w,\tau_w)=K_{const}(0.037e^{2.75CwCo}) \ (0.537|\tau_w|^{0.27})$$
(Equation 2)

K_{const} is the constant permeability coefficient of $2.0X10^{-10}$ m/s, C_w (mg/ml) the luminal surface LDL concentration and C_o (=1.3 mg/ml) the uniform constant LDL concentration at aortic arch inlet. The flow discharges were set according to Murray's law. A typical aortic arch blood flow waveform (resting condition) lasting 800 msec and shown in Figure 2 is applied over the entire ascending aorta entrance cross-section. Two characteristic time-points are selected for analysis; at 53.3 msec and refers to 0.17 m/s and at 336.7 msec with 0.05 m/s. The boundary conditions at the wall (endothelium), where n is the direction normal to the wall, can be described[2] as,

$$(C_w,V_w)-D\frac{\partial C}{\partial n}=KC_w$$
(Equation 3)

Results

Normalized luminal surface LDL concentration C_w/C_o contours at 0.05 m/s and 0.17 m/s are shown in Figures 3 and 4, respectively. In comparison to constant value model, shear dependent hydraulic conductivity exhibits increased LDL concentration. Table 1 shows the surface vertex average C_w/C_o for various endothelial property scenarios. Using V_w=0.6x10^{-8} m/s, K=2.0x10^{-10} m/s the surface vertex average C_w/C_o is 1.0425. The surface vertex average C_w/C_o is 1.0726 and 1.0848, at 336.7 msec and 53.3 msec time instants, respectively, for the shear dependent model. Peak C_w/C_o are 1.20 and 1.22 at 336.7 msec and 53.3 msec time instants, respectively. The concave side, compared to the convex one exhibits high LDL concentration. At the same time instant, the surface vertex average C_w/C_o over the entire normal aortic arch are 1.072 and 1.128 for the high (=50.0x10^{-12} m^2/s) and low molecular diffusivity (=25x10^{-12} m^2/s) values, respectively. Increased inlet blood flow yields elevated endothelial permeability. Peak endothelial permeability, using constant V_w for low and high inlet blood flow velocities, reaches 4.97x10^{-10} m/s and 5.74x10^{-10} m/s, respectively. For shear dependent V_w, the corresponding peak endothelial permeability values are 9.17x10^{-10} m/s and 12.9x10^{-10} m/s for low and high inlet blood flow velocities, respectively. High inlet blood flow velocity results into elevated V_w. As expected high V_w give rise to high WSS. Convex aortic arch regions expose high V_w and vice versa for the concave regions. Peak V_w for low and high inlet blood flow velocities reaches 1.71x10^{-8} m/s and 1.94x10^{-8} m/s, respectively.

Discussion

In the present research work experimental data of shear-dependent models for hydraulic conductivity and albumin permeability are used to numerically investigate the WSS influence on macromolecular accumulation in the aortic arch wall under oscillating flow conditions at rest. The amount of LDL transported to the arterial wall is a function of the luminal surface LDL elevation. High luminal surface concentration does not necessarily denote that all the LDL molecules will be transported through

Table 1. Statistics of surface vertex average C_w/C_o at cardiac cycle specific instants.

Time (msec)	Average inlet flow velocity (m/s)	V_w=0.6x10^{-8} K=2.0x10^{-10} (m/s)	V_w=0.6x10^{-8} shear dependent K (Equation 2) (m/s)	Shear dependent V_w (Equation1) K=2.0x10^{-10} (m/s)	Shear dependent V_w (Equation1), K (Equation2) (m/s)
53.3	0.17	1.04249	1.04158	1.08658	1.08485
336.7	0.05	1.04257	1.04217	1.07336	1.07259

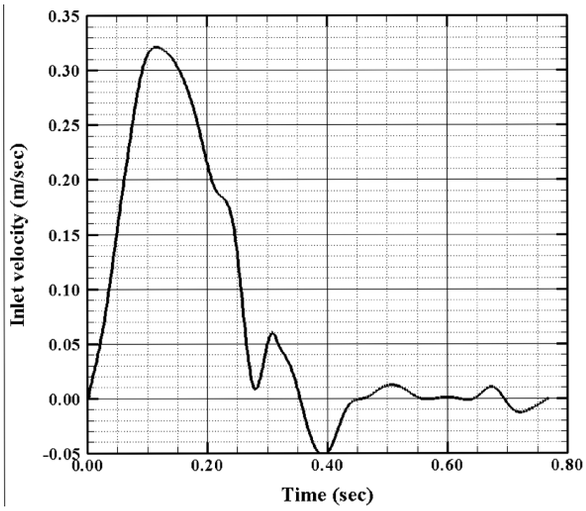

Figure 2: Average physiological human aortic arch velocity waveform. Computational analysis results refer to inlet flow velocities of 0.17 m/s and 0.05 m/s corresponding to waveform instants of 53.3 msec and 336.7 msec, respectively.

the vessel wall. It is generally considered that low WSS regions exhibit elevated LDL concentrations. The amount of LDL which finally passes is determined from the difference of the mass flow carried to the vessel wall by infiltration flow and the amount of flow which diffuses back to the main vessel flow[13], Equation 3.

It is apparent that increased V_w results into elevated LDL concentration. This does not contradict the fact that reduced WSS values exhibit reduced V_w, yielding lower LDL concentration. The WSS is a predominant factor in determining the LDL concentration. Cells try to minimize the side effects of increased LDL by reducing V_w wherever and whenever low WSS is encountered. The

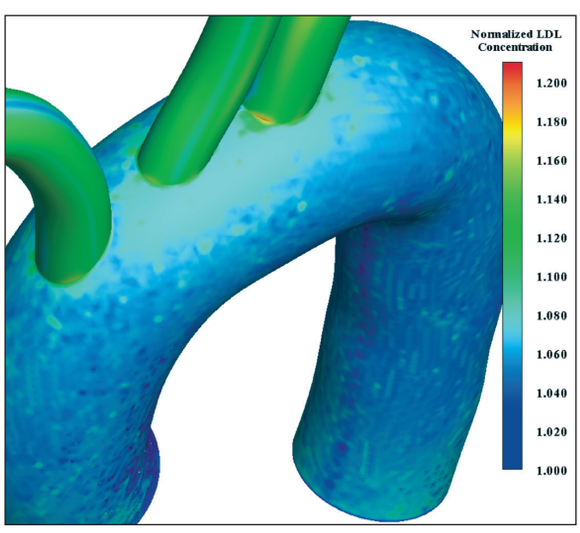

Figure 3: Normalized luminal surface LDL concentration C_w/C_o contours of the normal human aortic arch with shear dependent water infiltration and endothelial permeability, at 336.7 msec.

luminal surface LDL concentration is altered in the case of shear dependent V_w. Thus, the mass flow carried to the endothelium is higher. Infiltration flow increases LDL accumulation under low WSS[2] and reduces LDL under high WSS. Surface vertex average C_w/C_o using constant V_w and endothelial permeability is of 4.2 % order higher than that at the entrance. In case of shear dependent V_w, the surface vertex average C_w/C_o is 7.3 % higher than that at the entrance for low velocity inlet. At increased inlet velocity the above value reaches 8.5 %. Current results show that increased LDL diffusivity reduces the endothelial surface lipid concentration.

Arterial wall deformation needs to be taken into consideration, since the flow pattern-mass transport is largely determined by the geometrical configuration of the artery. Hypolipidaemic and antihypertensive agents

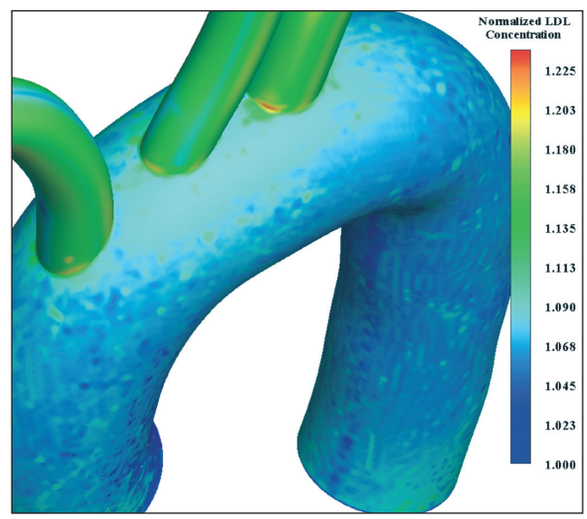

Figure 4: Normalized luminal surface LDL concentration C_w/C_o contours of the normal human aortic arch with shear dependent water infiltration and endothelial permeability, at 53.3 msec.

may affect the localization of aortic arch atherosclerotic regions; this possibility should be investigated. The percentage of LDL deposition at the surface of the endothelium, in terms of the circulating LDL quantity, needs to be analyzed.

Conclusion

The luminal surface LDL concentration at the arterial wall increases with the V_w rate through the vessel wall and decreases with increasing WSS rate. Concave sides of the aortic arch exhibit, relatively to the convex ones, elevated LDL at all time steps. At any instant of the cardiac cycle, the surface vertex average C_w/C_o is 4.25 % higher than that at the entrance (constant value model). With shear dependent V_w and endothelial permeability the surface vertex average C_w/C_o is 7.3 % higher than at the entrance (low inlet velocity). At the increased inlet velocity the above value reaches 8.5 %. The degree of

elevation in luminal surface LDL concentration is mostly affected from the V_w at vessel wall. The regional area of high luminal surface concentration is increased with increasing V_w velocity. Decreased molecular diffusivity increases the LDL concentration.

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