Simulation of the Effect of Tachycardia on Atherosclerotic Plaque Development Based on the LDL Transport in Coronary Arteries

Antonis I Sakellarios[1], Panagiotis K Siogkas[1], Vasilis D Tsakanikas[2], Kostas A Stefanou[2], Lampros K Michalis[3], Dimitrios I Fotiadis[2,3]

[1]Dept. of Materials Science and Engineering, University of Ioannina, Ioannina, Greece
[2] Biomedical Research Institute – FORTH, University Campus of Ioannina, Ioannina, Greece
[3] Medical School, Dept. of Cardiology, University of Ioannina, Ioannina, Greece

Abstract

In this work, the effect of high heart rate on the LDL transport in arteries is examined using the finite element method. The velocity profile is pulsatile, while the tachycardia case is assumed to have 40% increased flow rate and 25% increased velocity than the normal case. The Navier-Stokes equations are used to model the blood flow and LDL transfer is modeled using the convection-diffusion equation. The LDL accumulation is considered to be shear stress dependent. The results indicate the role of hemodynamics on the accumulation of LDL. Moreover, high heart rate enhances the influence of blood flow lengthening the exposure to low shear stress during systole. It is found that the area with low wall shear stress is about 8% greater in the tachycardia case than the normal case. The penetration of LDL on the arterial endothelium is increased at the systolic phase.

1. Introduction

Atherosclerosis is one of the main causes of death in western societies [1]. The development of the atherosclerotic plaque is associated with various factors such as hemodynamic and biological. Especially, the arterial wall is affected by the local hemodynamic conditions, which influence the permeability of the endothelium to biomolecules, cells or plasma. Furthermore, is it assessed that curves, bifurcations and other complex geometries are more prone for atherosclerotic plaque development [2]. Also, at these regions the wall shear stress is low which also enhances the process of atherosclerosis. On the other hand, atherosclerosis is affected by biological and biochemical factors such as the concentration of the Low Density Lipoprotein (LDL). The endothelial permeability is mainly affected by the molecule's size and its concentration [3]. Finally, experimental studies indicate the positive relation of the low wall shear stress and LDL accumulation in the arterial wall.

Since LDL transport from blood and accumulation into the arterial wall is the initial stage of the atherosclerotic plaque development, many studies focused on the mechanism of how LDL adheres and penetrates the endothelium. In particular the accumulation of LDL in the artery causes the development of a lipid core which initializes the progressive development of the plaque. The first studies are based on many assumptions and lacks accuracy. In particular, the main assumption is that the endothelial membrane is impermeable as well as the arterial geometries are represented by non realistic geometries [4]. Some studies model mass transfer in arteries using 2D models considering the arterial wall permeable [5]. The last years the models are more accurate using 3D realistic geometries which are reconstructed using the existed image modalities such as Intravascular Ultrasound, Angiography, Magnetic Resonance Imaging etc. Sun et al. [6,7] proposed a model for LDL transport in arteries using the Kedem-Katchalsky equations [8] to describe to transport across the endothelial membrane. Olgac et al. [9,10] presented a more complex model which considers three pathways for the LDL penetration increasing the complexity of the model and the need for experimental data.

Furthermore, it is reported by experimental studies that tachycardia or high heart rate affects the physiology of the arterial wall enhancing the pro-atherosclerotic conditions [11]. The endothelium is exposed to extended low shear stress period during the systolic phase. In this work, for first time the effect of high heart rate to atherosclerotic plaque development is studied. In particular, two case studies are used: 3D reconstructed right coronary artery with and without atherosclerotic plaque. Also, a normal and a tachycardia velocity profile are used to simulate the flow conditions. The model proposed by Sun et al. [6] is used to describe the arterial permeability. The simulation is performed using the finite

element method.

2. Methods

Simulations are performed in 3D reconstructed coronary arteries from IVUS and Bi-plane Angiography. The coronary artery with severe stenosis up to 75% is reconstructed manually in order to have this artery without the plaque. This model will be used as pro-atherosclerotic artery. Both arterial models are shown in Fig. 1.

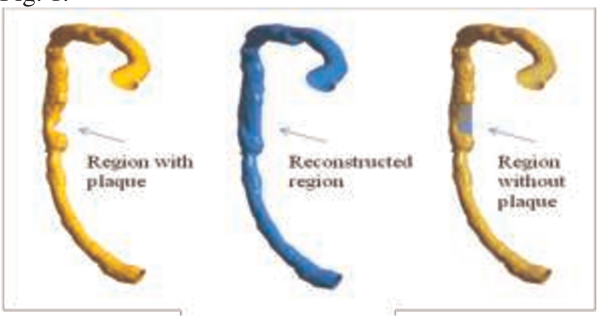

Figure 1. 3D reconstructed coronary arteries. Yellow indicates the original reconstructed artery, while the blue one depicts the manually reconstructed artery at the region of the plaque.

The 3D geometry models are discretized using 400,000 hexahedral elements. Furthermore, adaptive mesh is used to improve the mesh quality at the regions where high pressure variations exist.

2.1. Fluid dynamics

We assume that the blood is Newtonian, while the flow is laminar and incompressible. The blood flow is modelled using the Navier-Stokes equations and the continuity equation:

$$-\mu\nabla^2 \mathrm{v} + \rho(\mathrm{v}\cdot\nabla)\mathrm{v} + \nabla \mathrm{p} = 0 \quad (1)$$

$$\nabla \mathrm{v} = 0\,, \quad (2)$$

where v is the blood velocity, p is the pressure, μ is the viscosity of the blood and ρ is the blood density.

At the inlet we define transient velocity profile. In Fig. 2 both the normal and the tachycardia velocity profile are shown. The tachycardia case is assumed to have 40% increased flow rate and 25% increased velocity than the normal case. At the outlet zero pressure condition is defined.

2.2. Solute dynamics

We assume that the LDL size does not affect the flow and the endothelial permeability. The LDL

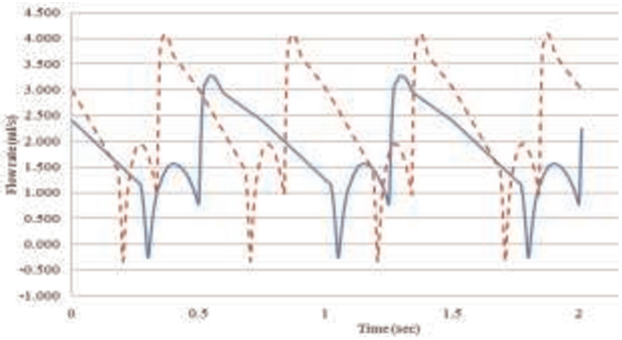

Figure 2. The blue line indicates the normal inlet flow profile, while the red dashed line indicates the tachycardia blood flow profile.

transport is modelled using the Convection-Diffusion equation:

$$\nabla\cdot(-\mathrm{D}\nabla \mathrm{c} + \mathrm{cv}) = 0\,, \quad (3)$$

where c is the concentration of the LDL and D is the LDL diffusivity in the arterial lumen. At the inlet, we assume constant LDL concentration is equal to 4.1 mol/m^3. At the outlet, convective flux boundary condition is applied.

2.3. Endothelial permeability

The endothelial permeability is modelled using the Kedem-Katchalsky equations [8]:

$$\mathrm{J_v} = \mathrm{L_p}(\Delta \mathrm{p} - \sigma_\mathrm{d}\Delta\pi) \quad (4)$$

$$\mathrm{J_s} = \mathrm{P}\Delta \mathrm{c} + (1-\sigma_\mathrm{f})\mathrm{J_v}\bar{\mathrm{c}}\,, \quad (5)$$

where $\mathrm{J_v}$ is the transmural velocity and $\mathrm{J_s}$ is the solute flux through endothelium, $\mathrm{L_p}$ is the hydraulic conductivity, $\Delta \mathrm{p}$ and $\Delta\pi$ are the pressure difference and the osmotic pressure difference across to endothelial membranes, respectively, c is the solute concentration, and σ_d, σ_f are the reflection coefficients.

The transmural velocity and the solute flux are applied as boundary conditions at the endothelial layer of the artery wall. In particular:

$$\mathrm{v}\mathbf{n} = \mathrm{J_v} \quad (6)$$

$$-\mathrm{D}\nabla \mathrm{c}\mathbf{n} + \mathrm{vc}\mathbf{n} = \mathrm{J_s}\,, \quad (7)$$

where $\mathbf{n}$ is the normal vector to the arterial wall.

3. Results

Simulations are performed in two coronary arteries: an

artery with plaque and one without plaque. Also, two inlet velocity profiles are used: a normal pulsatile profile and one which corresponds to tachycardia profile. In Fig. 3 contours of wall shear stress and LDL concentration are depicted at the time of the systole. In particular, Figs. 3a,b show the wall shear stress and LDL concentration, respectively. In contrast, Figs. 3c,d depict the tachycardia case. Comparing the two cases it is shown that the wall shear stress has mainly lower values in the tachycardia case than in the normal case. The LDL concentration is higher in the tachycardia case than the normal case.

The mean area of the low wall shear stress during the systolic phase is 13.7 10^{-5} m^2 (Figure 4a) in the case of the atherosclerotic artery. At this region, for the same time period, the average LDL concentration is 4.3 mol/m^3. On the other hand the mean area of the low wall shear stress at the tachycardia case is 14.8 10^{-5} m^2 (Figure 4b) corresponding to 8% increase of the high risk area. Furthermore, the average LDL concentration in the tachycardia case is 4.71% which corresponds to 10% increase. These results agree with experimental studies which refer that the average wall shear stress during systole is lower in tachycardia patients than in normal cases lengthening in that way the exposure to high risk hemodynamic factors for atherosclerotic plaque development [11-13].

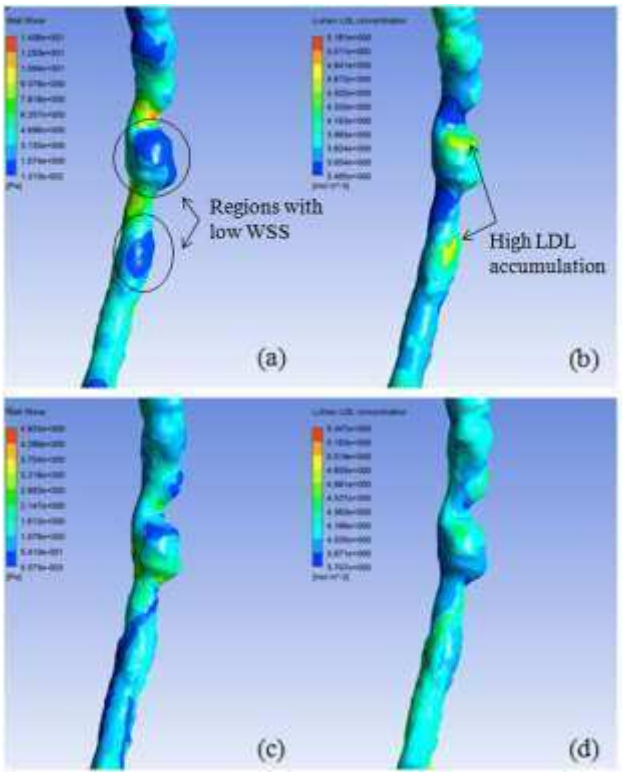

Figure 3. Contours a and c depict the wall shear stress for the normal and tachycardia case, respectively. Contours b and d show the LDL concentration for the normal and tachycardia case, respectively.

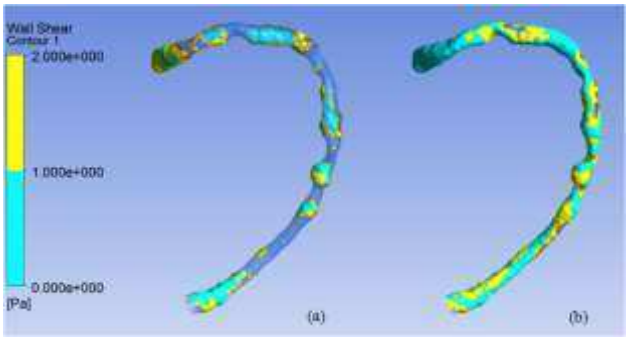

Figure 4. Area of low wall shear stress at the normal (a) and tachycardia (b) case.

Comparing the models with the plaque and the reconstructed artery without plaque, we observe significant differences at the blood velocity streamlines at the region of interest (region with or without plaque). That also affects the accumulation of LDL, which is increased at the regions of disturbed flow as it is depicted in Fig. 5. In particular, the flow at the reconstructed artery is not disturbed as in the atherosclerotic artery and thus the distribution of LDL molecules is made uniformly. On the other hand the accumulation of LDL after the region of the atherosclerotic plaque is increased which causes its further progression.

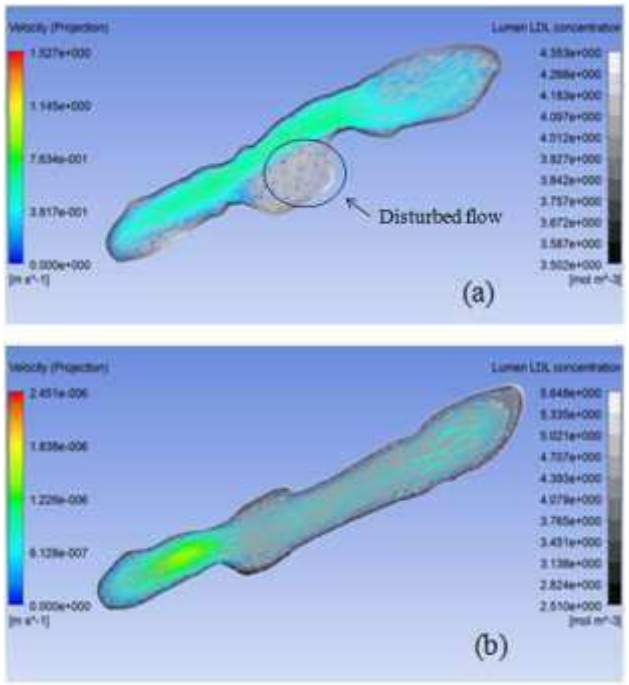

Figure 5. Velocity streamlines (rainbow color map) and LDL concentration (grey scale color map) at the atherosclerotic region of the artery.

4. Discussion – conclusions

We study for the first time the effect of tachycardia on the

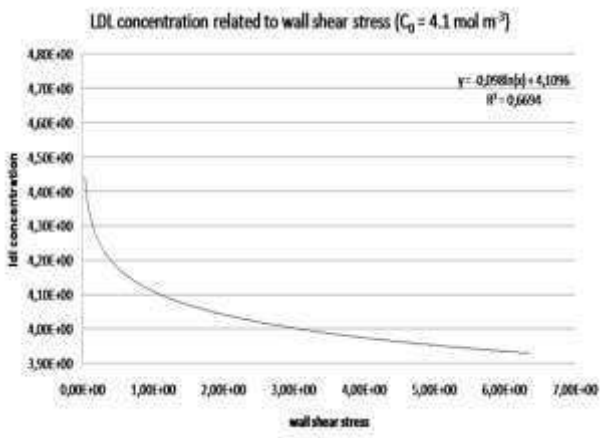

Figure 6. The relation of LDL concentration to the wall shear stress.

LDL accumulation in arteries and the atherosclerotic plaque development. The finite element method is used for the simulations which are performed on 3D patient-specific coronary arterial models reconstructed using IVUS and angiography. The arterial wall is considered to be impermeable and the Kedem-Katchalsky equations are used to model the LDL penetration. Comparison is made between the normal and tachycardia blood flow cases. Also, the effect of the disturbed flow is examined at the region of the developed atherosclerotic plaque. The results also confirm the assumption of the wall shear stress dependent endothelial permeability which is defined at the endothelial layer. In Fig. 6 the relation of LDL concentration to the wall shear stress is depicted. The LDL molecules accumulate at the regions of wall shear stress as well as at the regions of disturbed flows.

Concluding, tachycardia plays a role to atherosclerotic plaque development. In particular, the exposure to low wall shear stress is increased in high heart rates. Furthermore, in normal situations the ratio of diastole vs. systole duration is 2:1 [11]. However, in the case of tachycardia, the diastole duration is degraded and thus the exposure to atherogenic effect of the systole increases. Finally, our model needs further improvement. Especially, the fluid-structure interaction must be included, since variations of the heart rate also affect the arterial wall by increasing the magnitude of the mechanical load imposed on it. Finally, experimental studies indicate that the influence of hemodynamic factors in gene expression must be modelled.

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Address for correspondence.

Dimitrios I. Fotiadis
Unit of Medical Technology and Intelligent Information Systems, Dept. of Materials Science and Engineering, University of Ioannina, GR 451 10 Ioannina, GREECE.
fotiadis@cs.uoi.gr