Early Atherosclerosis Process: Mathematical Modeling and Numerical Simulations

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Abstract

The early stage of atherosclerosis disease - low density lipoproteins (LDL) transport across the endothelium barrier; the LDL oxidation process inside the subendothelial layer and the monocytes adhesion and transmigration - is a fundamental phase of the atherosclerosis, which should be better understood from both the biological and mathematical modeling perspectives.

In this talk we will present a mathematical model which describes the development of the early atherosclerotic lesions. The model assumes that a given quantity of LDL in the lumen transported with blood plasma will accumulate on the endothelial cells (EC) surface, due to the blood flow behavior (region of low wall shear stress) [1]. Elevated LDL concentration on the EC surface will lead to changes in the endothelial permeability, creating the leaky junctions which is the main pathway to the accumulation of LDL into the tunica intima [2],[3], [1]. Intra intimal LDL undergoes oxidized (oxLDL) by oxidant mechanisms [4]. High concentration of oxidized LDL leads to anti-inflammatory reaction: monocytes adhere to the endothelium and migrate into the intima, under the influence of chemoattractant molecules, where they differentiate into active macrophages in order to phagocyte the oxLDL [5], [6], [4].

The blood flow in the lumen is governed by the Navier-Stokes equations and the tunica intima is considered as a poroelastic medium, with the dynamics described by the Biot system [7]. Convection-diffusion-reaction (CDR) equations are used to model the concentrations of LDL and monocytes in the lumen as well as in the intima. The inflammatory process inside the intima is essentially described by CDR equations.

Numerical simulations are performed in an idealized two-dimensional geometry, with a simplified model in order to study the transport of LDL and monocytes across the endothelium, and the changes in the endothelial permeability due to the high concentration of LDL on the EC surface and due to the inflammatory process.

Keywords: Early atherosclerosis, low density lipoproteins, monocytes, cytokines, endothelial permeability, wall shear stress, convection-diffusion-reaction equations.

References

[1] M. Colic, S. Pantovic, M. Jeremic, V. Jokovic, Z. Obradovic and M. Rosic, Transport of Low-Density Lipoprotein Into the Blood Vessel Wall During Atherogenic Diet in the Isolated Rabbit Carotid Artery, *Circulation Journal*, **79** (2005), 1846-1852.

[2] L. M. Cancel, A. Fitting and J. M. Tarbell, In vitro study of LDL transport under pressurized (convective) conditions, *Am J Physiol Heart Circ Physiol*, **293** (2007), H126-H132.

[3] X. Xie, J. Tan, D. Wei, D. Lei, T. Yin, J. Huang, et al., In vitro and in vivo investigations on the effects of low-density lipoprotein concentration polarization and haemodynamics on atherosclerotic localization in rabbit and zebrafish, *J. R. Soc. Interface*, **10** (2012), 1-11.

[4] A. N. Orekhov, Y. V. Bobryshev, I. A. Sobenin, A. A. Melnichenko and D. A. Chistiakov, Modified Low Density Lipoprotein and Lipoprotein-Containing Circulating Immune Complexes as Diagnostic and Prognostic Biomarkers of Atherosclerosis and Type 1 Diabetes Macrovascular Disease, *Int. J. Mol. Sci.*, **15** (2014), 12807-12841.

[5] S. Mitra, T. Goyal and J. L. Mehta, Oxidized LDL, LOX-1 and Atherosclerosis, *Cardiovasc Drugs Ther*, **25** (2011), 419-429.

[6] S. Frank and G. Kostner (Editors), *Lipoproteins - Role in Health and Diseases*, INTECH Open Access Publisher, 2012.

[7] S. Badia, A. Quaini, A. Quarteroni, Coupling Biot and Navier-Stokes equations for modelling fluid-poroelastic media interaction, *J. Comput. Phys.*, **228** (2009) 7986-8014.