Computers & Fluids xxx (2013) xxx–xxx

Contents lists available at SciVerse ScienceDirect

Computers & Fluids

journal homepage: www.elsevier.com/locate/compfluid

Computer simulation of three-dimensional plaque formation and progression in the coronary artery

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ARTICLE INFO

Article history:
Received 2 March 2013
Received in revised form 24 June 2013
Accepted 8 July 2013
Available online xxxx

Keywords:
Atherosclerosis
Computer model
Animal experiment
Patient data

ABSTRACT

Atherosclerosis is a progressive disease characterized by inflammation and lipid accumulation in the vascular wall. In this study, we analysed animal experiments and clinical data for plaque formation and progression. The first animal experiment examined cast model on the carotid artery (Cheng et al., 2006) [21]. The second animal experiment is related for pig on the left anterior descending coronary artery (LAD) after 2 month of high fat diet. Experimental model of plaque formation on pig LAD is simulated numerically using specific animal data obtained from intravascular ultrasound (IVUS) and histological data. The 3D blood flow is governed by the Navier–Stokes equations, together with the continuity equation. Mass transfer within the blood lumen and through the arterial wall is coupled with the blood flow and is modeled by the convection–diffusion equation. LDL transport in lumen of the vessel is described by Kedem–Katchalsky equations. The inflammatory process is solved using three additional reaction–diffusion partial differential equations. Lipids concentration in the intimal area of the low shear stress was 16% and for oscillatory zone 10% which is in good agreement with experimental data. Computed concentration of macrophages for pig model indicates that there is a newly formed matter in the intima, especially at foam cell lipids area which varied from 12% to 20% and chemokine receptor type 4 (CXCR4) areas from 1.5% to 3.5%. Patients' study predicts new plaque formation after 12 months follow up which corresponds to size and plaque composition. Matching of plaque location, size and composition progression in time between experimental and computer model shows a potential benefit for future prediction of this vascular decease.

1. Introduction

Atherosclerosis is a progressive disease characterized by the accumulation of lipids and fibrous elements in the large arteries. In the last decade, scientists come to appreciate a prominent role for inflammation in atherosclerosis. Formerly focused on luminal narrowing due to the bulk of atheroma, the current concepts recognize the biological attributes of the atheroma as key determinants of its clinical significance [1].

Inflammatory process starts with penetration of low density lipoprotein (LDL) in the intima. This penetration, if too high, is followed by leucocyte recruitment in the intima. One endothelial-leukocyte adhesion molecule has emerged as a particularly attractive candidate for the early adhesion of mononuclear leukocytes to arterial endothelium at sites of atheroma initiation: Vascular cell adhesion molecule-1 (VCAM-1). This process may participate in formation of the fatty streak, the initial lesion of atherosclerosis and then in formation of a plaque [2] (see Figs. 1 and 2).

Several mathematical models have recently been used for the transport of macromolecules, such as low-density lipoprotein, from the arterial lumen to the arterial wall and inside the wall [4–6]. These models are usually classified in three categories according to the level of description of the arterial wall. The simplest model is called the wall-free model, since in this model the arterial wall is simply described by means of an appropriate boundary condition. Kaazempur-Mofrad and Ethier [2] simulated the mass transport in a realistic human right coronary artery and Wada et al. [7] used a wall-free model to study the concentration polarization phenomenon. The wall-free model does not provide any information on the transmural flow and solute dynamics in the arterial wall. The fluid-wall models that can be either single-layer or multilayer for the solute dynamics not only in the lumen, but also in the arterial wall. Stangeby and Ethier [8] analysed the wall as single layer porous medium and solved the coupled luminal blood flow and transmural fluid flow using Brinkman's equations. Al and Vafai [9] used multilayer models which represent intima

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http://dx.doi.org/10.1016/j.compfluid.2013.07.006

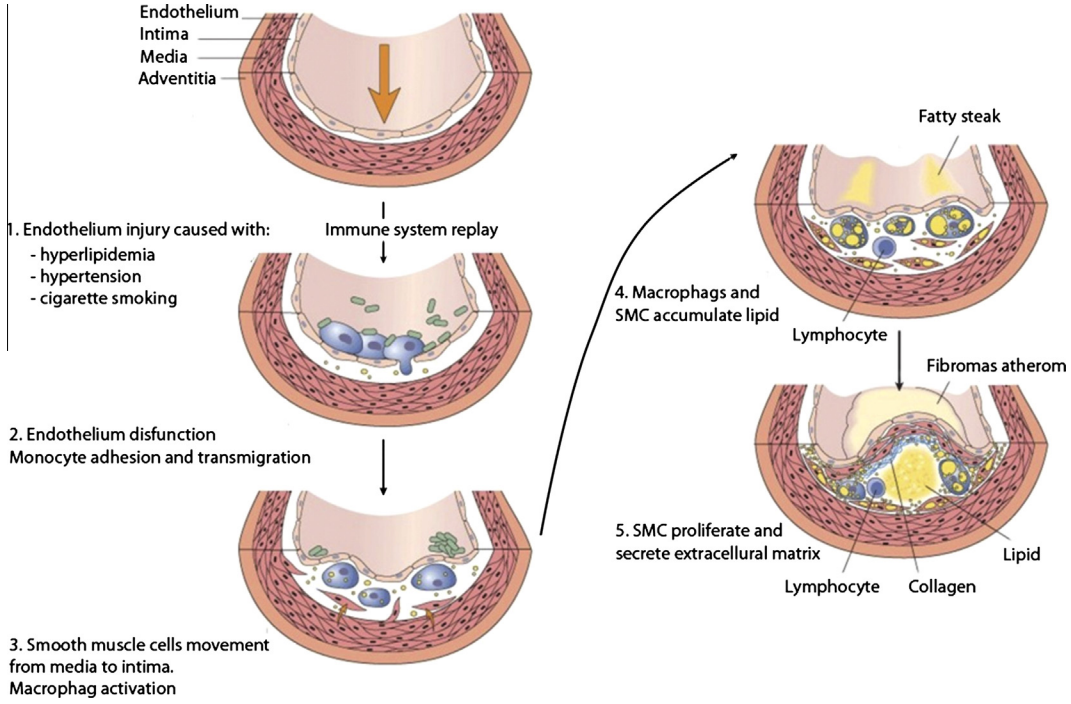

Fig. 1. Development of the atherosclerotic plaque (adapted from [3]).

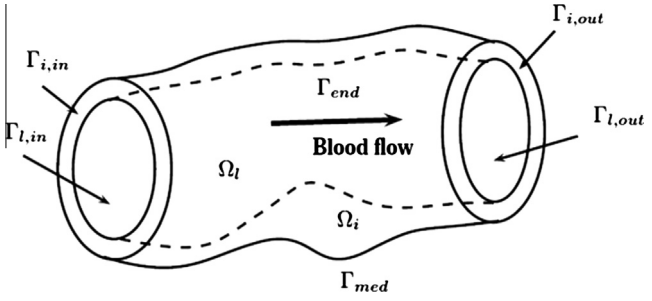

Fig. 2. Geometry of the problem.

and media separately. Olgac et al. [10] used a three-pore model for LDL transport. Crosseto et al. [11] used finite elements simulation of the fluid–structure interaction between blood flow and arterial wall deformation of a healthy aorta. It is now well known that the early stage of the inflammatory disease is the result of interaction between plasma low density lipoproteins that filtrate through endothelium into the intima, cellular components (monocytes/macrophages, endothelial cells and smooth muscle cells) and the extracellular matrix of the arterial wall [12].

In this study we performed computational study for plaque initial progression and composition. The aim is to connect LDL transport with macrophages and oxidized LDL distribution as well as initial plaque growth model inside the intimal area. We firstly described mass transport of LDL through the wall and the simplified inflammatory process. The Navier–Stokes equations govern the blood motion in the lumen, the Darcy law is used for model blood filtration, Kedem–Katchalsky equations [13,14] for the solute and flux exchanges between the lumen and the intima. Then we described the system of three additional reaction-diffusion equations that models the inflammatory process and lesion growth model in the intima. This model relies on a matter incompressibility assumption. The next sections are devoted to numerical simulation examples for animal model in three dimension domain and comparison with experimental results from literature and our own experimental data. Also we gave initial results for clinical data for the coronary artery. At the end some discussion and conclusions remarks are described.

2. Materials and methods

2.1. Mass transfer problem

In this section we firstly present mass transfer problem for LDL transport through the wall and then a continuum based approach for plaque formation and development in three-dimension is described. The governing equations and numerical procedures are given. The blood flow in lumen domain is simulated by the three-dimensional Navier–Stokes equations, together with the continuity equation

$$-\mu\nabla^2 u_l + \rho(u_l \cdot \nabla)u_l + \nabla p_l = 0 \tag{2.1}$$

$$\nabla u_l = 0 \tag{2.2}$$

where u_l is blood velocity in the lumen, p_l is the pressure, μ is the dynamic viscosity of the blood, and ρ is the density of the blood.

Mass transfer in the blood lumen is coupled with the blood flow and modeled by the convection–diffusion equation as follows

$$\nabla \cdot (-D_l \nabla c_l + c_l u_l) = 0 \tag{2.3}$$

in the fluid domain, where c_l is the solute concentration in the blood domain, and D_l is the solute diffusivity in the lumen.

Mass transfer in the arterial wall is coupled with the transmural flow and modeled by the convection–diffusion–reaction equation as follows

$$\nabla \cdot (-D_w \nabla c_w + k c_w u_w) = r_w c_w \tag{2.4}$$

in the wall domain, where c_w is the solute concentration in the arterial wall, D_w is the solute diffusivity in the arterial wall, k is the solute lag coefficient, and r_w is the consumption rate constant.

LDL transport in lumen of the vessel is coupled with Kedem–Katchalsky equations [13,14]:

Please cite this article in press as: Filipovic N et al. Computer simulation of three-dimensional plaque formation and progression in the coronary artery. Comput Fluids (2013), http://dx.doi.org/10.1016/j.compfluid.2013.07.006