Journal of Biomechanics 44 (2011) 2466–2471

Contents lists available at ScienceDirect

Journal of Biomechanics

journal homepage: www.elsevier.com/locate/jbiomech
www.JBiomech.com

Computed high concentrations of low-density lipoprotein correlate with plaque locations in human coronary arteries

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ARTICLE INFO

Article history:
Accepted 15 June 2011

Keywords:
LDL transport
Patient-specific simulations
Atherosclerosis
Computational fluid dynamics
Computed tomography

ABSTRACT

Subendothelial accumulation of low-density lipoprotein (LDL) in arterial walls is an initiator of atherosclerotic plaque formation. We report here on the correlation between healthy state subendothelial LDL concentration distribution and sites of subsequent plaque formation in coronary arteries of patients with coronary artery disease (CAD). We acquired left (LCA) and right coronary artery (RCA) and atherosclerotic plaque geometries of 60 patients with CAD using dual-source computed tomography angiography. After virtually removing all plaques to obtain an approximation of the arteries' healthy state, we calculated LDL concentration in the artery walls as a function of local lumen-side shear stress. We found that maximum subendothelial LDL concentrations at plaque locations were, on average, 45% (RCA) and 187% (LCA) higher than the respective average subendothelial concentration. Our results demonstrate that locally elevated subendothelial LDL concentration correlates with subsequent plaque formation at the same location.

1. Introduction

Atherosclerotic plaque formation appears at the end of a chain of events that starts with subendothelial retention of low-density lipoprotein (LDL) in arterial walls, followed by LDL accumulation, LDL oxidation, entry of monocytes into the wall and subsequent formation of foam cells (Lusis, 2000; Skalen et al., 2002). Tompkins et al. (1989) showed in squirrel monkeys that there are focal regions of high LDL concentration throughout the cardiovascular system. It has also been shown by Schwenke and Carew (1989) that LDL concentration is higher in generally lesion-prone sites in cholesterol-fed rabbit aortas compared to lesion-resistant sites. A more recent autopsy study of children and young adults who died of non-cardiac causes showed initial stages of atherosclerosis at various locations in the right coronary arteries and reported the density distribution of lipids and macrophages in these locations (Nakashima et al., 2007). However, there is thus far no study that documents LDL concentration in actual plaque locations prior to plaque formation. In the work at hand, we reconstruct the approximate healthy state anatomy of the coronary arteries of 60 patients with atherosclerotic plaques, compute the LDL concentration distribution in the artery walls and correlate it with the actual plaque locations. LDL concentrations are obtained using a previously published approach (Olgac et al., 2009), in which the endothelium is represented by a three-pore model (Olgac et al., 2008) that enables the inclusion of the effects of local wall shear stress (WSS) on various pathways of LDL and blood plasma fluxes. Concretely, low wall shear stress increases the turnover rate of endothelial cells, thereby increasing the local density of leaky junctions and with it the corresponding LDL and blood plasma fluxes. The novelty of this patient study lies in the quantification of the thus far only qualitatively described relationship between subendothelial LDL concentration and plaque formation.

2. Methods

Right and left coronary arteries of 30 patients were each studied independently. The RCA patient population consisted of 80% (24/30) males with an average age and body mass index (BMI) of 67.1 ± 9.2 years (47–84) and 26.3 ± 4.3 kg/m^2 (15.6–36.3), respectively. The left coronary patient population consisted of 70% (21/30) males with an average age and body mass index (BMI) of 64.8 ± 10.3 years (43–82) and 25.3 ± 3.1 kg/m^2 (20.3–32.8), respectively. Demographic data and clinical characteristics of the two patient groups are summarized in Table 1.

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doi:10.1016/j.jbiomech.2011.06.022