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Three-dimensional numerical simulation of blood flow in mouse aortic arch around atherosclerotic plaques ☆

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ABSTRACT

Atherosclerosis is a progressive disease, involving the build-up of lipid streaks in artery walls, leading to plaques. Understanding the development of atherosclerosis and plaque vulnerability is critically important since plaque rupture can result in heart attack or stroke. Plaques can be divided into two distinct types: those likely to rupture (vulnerable) or less likely to rupture (stable). In the last decade, researchers have been interested in studying the influence of the mechanical effects (blood shear stress, pressure forces and structural stress) on the plaque formation, progression and rupture processes but no general agreement has been found. The purpose of the present work is to include more realistic conditions for the numerical calculations of the blood flow by implementing real geometries with plaques in the numerical model. Hemodynamical parameters are studied in both diseased and healthy configurations. The healthy configuration is obtained by removing numerically the plaques from three dimensional geometries obtained by micro-computed tomography. A new hemodynamical parameter is also introduced to relate the location of plaques to the characteristics of the flow in the healthy configuration.

1. Introduction

Atherosclerosis is an inflammatory disease characterized by lipid and macrophages accumulation underneath the endothelium at the boundary of blood vessel walls. In addition to lipid deposition, atherosclerotic progression involves a complex process of monocyte infiltration, lipid oxidation, foam cell formation, smooth muscle cell migration and extracellular matrix production [1–3]. The lipid core is separated from the circulating blood by a fibrous cap composed of smooth muscle cells and extracellular matrix [2]. As plaques develop, they can cause luminal narrowing (reduction of the volume of the fluid

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Nomenclature

Abbreviations

BCA	brachiocephalic artery
LCC	left common carotid artery
LDL	low density lipoproteins
LS	left subclavian artery
μ-CT	micro-computed tomography
OSI	oscillatory shear index
RRT	relative residence time
TAGP	time average gradient of pressure
TAWSS	time average wall shear stress
WSSG	wall shear stress gradient
WSS	wall shear stress

Greek symbols

μ	dynamic viscosity
ρ	density
τ_w	instantaneous wall shear stress

part), or may undergo expansive remodeling to maintain lumen diameter [4,5]. Vulnerable plaques are prone to rupture, with disruption of the fibrous cap exposing the thrombogenic plaque core to the circulating blood [6]. Interactions between platelets and the lipid core can induce thrombus formation on the plaque surface, with possible consequences including vessel occlusion, myocardial infarction or stroke. While it is accepted that plaque vulnerability is influenced by fibrous cap thickness and the size of the lipid core [7], it also depends on biochemical factors, luminal remodeling and hemodynamic parameters for which no general agreement has been found [8,9].

Atherosclerotic plaques are found at particular sites in the arterial tree [10], with plaques commonly found on the inner curvatures of arteries and near bifurcations. This regional localization of atherosclerosis depends largely on hemodynamic factors such as wall shear stress (WSS) [2]. The distribution of the hemodynamic field depends on the geometrical patterns of the arteries, with low time averaged wall shear stress (TAWSS) commonly observed on inner curvatures of arteries and oscillatory TAWSS of low amplitude in regions of bifurcations [11]. This low WSS hypothesis for plaque formation and progression has been proposed by numerous groups [4,12–14] and has been related to the alteration of cholesterol transport [15]. In the regions of disturbed flow, the shape and direction of endothelial cells change and consequently does the permeability of the endothelial layer to external molecules [16,17]. In Liu et al. [18], the authors suggest that the concentration polarization of the low density lipoproteins (LDLs) and some specific aortic arch geometrical features are involved in the localization of the atherogenesis. Other hemodynamic factors are also thought to play a role in plaque development including the oscillatory shear index (OSI) [19–21], which quantifies the cyclic departure of the WSS vector from its predominant axial alignment, the wall shear stress gradient (WSSG) corresponding to spatial WSS variation [22,23], and the relative residence time (RRT) corresponding to a relative time spent by a particle at a specific site near the wall [24]. It is noticeable that the optimal hemodynamical parameter to relate subject specific physiological characteristics and plaque formation has not been agreed upon [25]. This uncertainty may be due to the fact that most of the studies that investigate the processes of early stage plaque formation consider healthy arteries and draw their conclusions assuming that plaques will grow in the most likely sites referenced in the literature. Thus, while it is largely agreed that atherosclerotic development occurs in regions of disturbed flow, the exact contributions of various hemodynamic parameters such as TAWSS, OSI, WSSG and RRT are still under debate.

In a similar way, the plaque growth process is poorly understood and the link with the mechanical effects not well identified. A limited number of recent studies [13,26–30] consider the details of processes of the growth of plaques after their initiation and, in particular, the influence of their presence on the blood flow. While researchers have attempted to correlate the plaque growth to hemodynamical factors, general conclusions cannot be drawn yet from these studies. Wong et al. [31] have suggested the potential implication of the structural stresses in plaque progression for a model carotid geometry, whereas Olgac et al. [28] propose the study of the LDL transport to understand the plaque expansion in the coronary arteries. In Olgac et al. [28], the authors numerically remove the plaques in order to compare the dynamics of the LDL transport and blood flow in effectively the same artery for healthy and disease state. In the present paper, a similar approach is used. A discussion is conducted on the validity and limitations of this approach. In addition, the present paper aims to develop a methodology to better understand the two questions of plaque formation and progression by investigating the hemodynamics of blood flow through the mouse aortic arch with and without plaques. Two mouse models are being studied: wild type C57/B6 mice (no plaque) and ApoE deficient mice (stable plaques). After the tissues have been fixed, the samples (mice aortic arch)

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