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Computational fluid dynamics in coronary artery disease

Zhonghua Sun[a], Lei Xu[b,*]

[a] Discipline of Medical Imaging, Department of Imaging and Applied Physics, Curtin University, Perth, Western Australia 6845, Australia
[b] Department of Radiology, Beijing Anzhen Hospital, Capital Medical University, Beijing, China

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ABSTRACT

Computational fluid dynamics (CFD) is a widely used method in mechanical engineering to solve complex problems by analysing fluid flow, heat transfer, and associated phenomena by using computer simulations. In recent years, CFD has been increasingly used in biomedical research of coronary artery disease because of its high performance hardware and software. CFD techniques have been applied to study cardiovascular haemodynamics through simulation tools to predict the behaviour of circulatory blood flow in the human body. CFD simulation based on 3D luminal reconstructions can be used to analyse the local flow fields and flow profiling due to changes of coronary artery geometry, thus, identifying risk factors for development and progression of coronary artery disease. This review aims to provide an overview of the CFD applications in coronary artery disease, including biomechanics of atherosclerotic plaques, plaque progression and rupture; regional haemodynamics relative to plaque location and composition. A critical appraisal is given to a more recently developed application, fractional flow reserve based on CFD computation with regard to its diagnostic accuracy in the detection of haemodynamically significant coronary artery disease.

1. Introduction

Coronary artery disease is the leading cause of morbidity and mortality in advanced countries and its prevalence is increasing in developing countries. Coronary artery disease is responsible for 7.3 million deaths and 58 million disability-adjusted life years lost worldwide [1]. Despite its large socio-economic impact, the underlying mechanisms of coronary artery disease are only partially understood. It is generally accepted that coronary artery disease is an inflammatory disease with lipid deposition in the arterial wall as an initial stage of atherosclerosis [2–5]. Although the risk factors for atherosclerotic coronary plaque formation, including high cholesterol, diabetes, and hypertension are systemic in nature, plaques are located at specific sites in the coronary artery where disturbed flow and low endothelial shear stress occur (Fig. 1) [6–9].

In recent years, blood flow/shear stress has gained a lot of interest as complementary explanation for plaque formation [10,11]. The role of blood flow in the development of atherosclerosis is based on the observation that vascular inflammation and plaques are distributed near side branches or arterials stenosis, where blood flow is non-uniform, and at the lesser curvature of bends where blood flow rate is relatively low [12,13]. The effect of blood flow on the vessel wall is through shear stress, which influences the behaviour of endothelial cells including morphological adaptations and physiological changes of endothelial cells. Shear stress induces a shearing deformation of the endothelial cells which affects the phenotype of the endothelial cells and therefore the inflammatory component and plaque progression [14].

Low and oscillatory shear stress represent major features of the haemodynamic environment of regions opposite to arterial flow dividers that are predisposed to the formation of atherosclerosis (Fig. 2) [15–19]. It has been shown in vitro and in vivo studies that disturbed or oscillatory flows near arterial bifurcation, branch ostia and curvatures are associated with atheroma formation and intimal wall thickening [20–25]. The methods for in vivo estimation of wall shear stress can be performed by acquiring three-dimensional (3D) reconstruction of vessel volume using either invasive modalities such as intravascular ultrasound and invasive coronary angiography, or less-invasive techniques including coronary computed tomography angiography and cardiac magnetic resonance angiography with application of numerical methods to calculate flow within the reconstructed arterial volume for solving fluid dynamics [26,27]. The numerical methods are known as computational fluid dynamics (CFD) techniques.

3D reconstruction of coronary artery tree with subsequent numerical simulation using CFD techniques based on individual

* Corresponding author at: Department of Radiology, Beijing Anzhen Hospital, Capital Medical University, No. 2, Anzhen Road, Chaoyang District, 100029 Beijing, China. Tel.: +86 10 64456071; fax: +86 10 64456962.
E-mail addresses: z.sun@curtin.edu.au (Z. Sun), leixu2001@hotmail.com (L. Xu).

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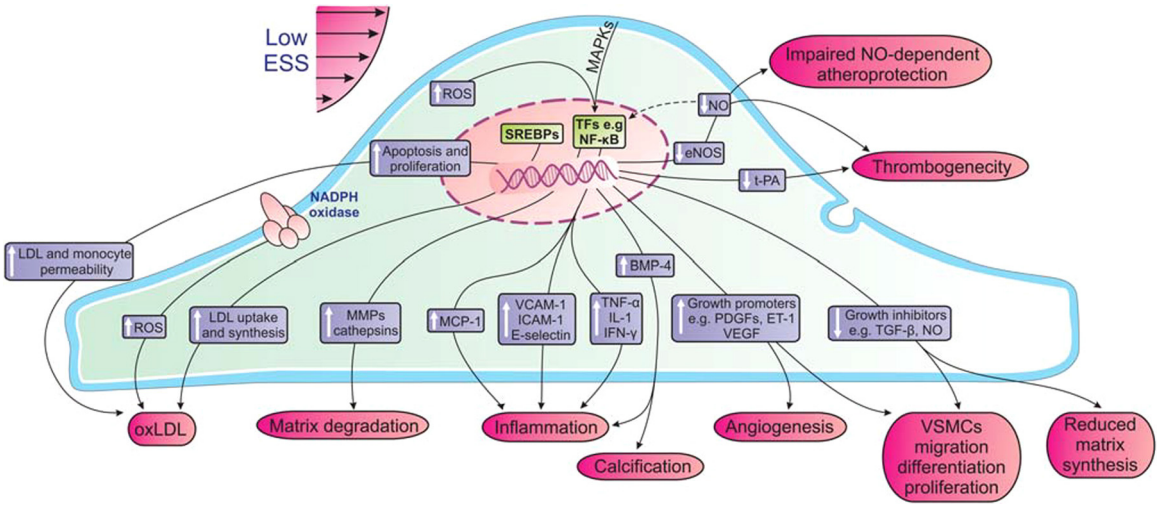

Fig. 1. Molecular and cellular mechanisms through which low ESS promotes atherosclerosis. Data are derived from in vitro and animal in vivo experiments by applying a great variety of ESS patterns, both in direction and in magnitude. ESS, endothelial shear stress; BMP, bone morphogenic protein; eNOS, endothelial nitric oxide syntase; ET, endothelin; ICAM-1, intercellular adhesion molecule 1; IFN-g, interferon-g; IL, interleukin; LDL, low-density lipoprotein cholesterol; MCP, monocyte chemoattractant protein; MMP, matrix metalloproteinase; NF kB, nuclear factor-kB; NO, nitric oxide; PDGF, platelet-derived growth factor; ROS, reactive oxygen species; SREBP, sterol regulatory elements binding protein; TF, transcription factor; TGF-b, transforming growth factor b; TNF-a, tumour necrosis factor-a; t-PA, tissue plasminogen activator; VCAM, vascular cell adhesion molecule; VEGF, vascular endothelial growth factor; VSMC, vascular smooth muscle cell.
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patient data is being increasingly used to study haemodynamics and in predicting the behaviour of circulatory blood flow inside the coronary arteries [28–30]. This review article provides an overview of the applications of CFD in the diagnosis of coronary artery disease. The main focus of this review is to present an evidence-based review of the CFD in the biomechanics of atherosclerotic plaques and in the detection of high-risk coronary plaques and plaque progression with the aim of identifying high-risk patients so as to achieve the goal of reducing cardiac mortality.

2. Computational fluid dynamics

CFD is a general term of all numerical techniques that are used to describe and analyse the flow of fluid elements at each location in certain geometry. The merit of CFD is developing new and improved devices and system designs, and optimisation is conducted on existing equipment through computational simulations resulting in enhanced efficiency and lower operating costs [31]. The governing equations of fluid dynamics can be computed to obtain coronary flow and pressure. These equations are called the Navier–Stokes equations and have been known for more than 150 years. In order to simulate realistic coronary blood flow, a domain of interest must be defined, and boundary conditions specified. The isolation and generation of boundary condition is one of the greatest challenges in the integration of CFD for the assessment of the physiologic significance of coronary artery disease [32].

The coronary arterial wall is constantly exposed to both flow-induced wall shear stress (WSS) and arterial strain (relative displacement of wall within coronary artery) by blood pressure, myocardial contraction and local biological environment. Haemodynamic parameters of WSS, such as average wall shear stress (AWSS), average wall shear stress gradient (AWSSG), oscillatory shear index (OSI) and relative residence time (RRT) are possible indicators for atherosclerotic plaque prone sites [33–36]. Of these parameters, low WSS or OSI is a well-described mechanical stimulus that promotes the inflammatory process by inducing an oxidative response in endothelial vascular cells [37]. Lowering WSS has been reported to induce structural responses, according to several studies performed on cultured endothelial cells [38–40]. Thus, vascular remodelling is a response to alterations in WSS and

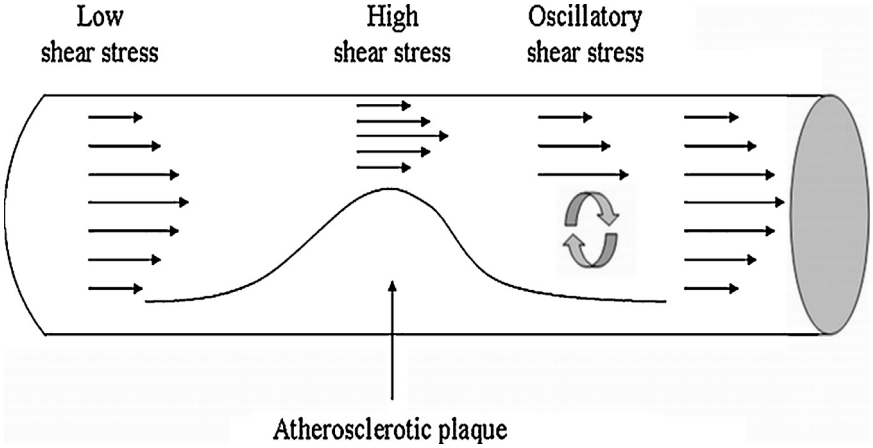

Fig. 2. Differential distribution of shear stress in a straight arterial segment proximal to a lumen-protruding atherosclerotic plaque.
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