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On the influence of variation in haemodynamic conditions on the generation and growth of cerebral aneurysms and atherogenesis: A computational model

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Abstract

A risk-factor criterion, based on near-wall haemodynamic conditions, for the assessment of vascular pathology risk is developed and tested. This criterion has its foundation on experimentally observed vascular wall responses to oscillatory and swirling wall shear stress patterns and is applied to the results of computational simulations. We test this model on two anatomically accurate vascular segments, where pathologies are either commonplace or have already been developed, i.e. a healthy carotid bifurcation and a cerebral fusiform aneurysm. In the case of the former, the risk-assessment criterion predicts the emergence of atherosclerosis of the same locations that the disease is usually encountered. In the case of the latter, the risk factor shows increased probability for the appearance of secondary, "baby", aneurysms at certain locations.

Keywords: Risk factor; Atherosclerosis; Cerebral aneurysms; Computational modelling

1. Introduction

While cerebral aneurysm pathology and atherosclerosis are two of the most common lesions of the cardiovascular system, there is no clear understanding on their pathogenesis mechanisms. A crucial step in the development of new treatment strategies is the understanding of the role of the haemodynamics in the process. The occurrence of atherosclerotic plaques (Texon, 1990) and cerebral aneurysms (Resnick et al., 2003) in well-recognized arterial regions, along with their focal distribution in regions of curvature, bifurcation and branching of the vessels, suggests that fluid dynamics play a pivotal role in the localization of those lesions. Studies suggest that low wall stress and high oscillatory patterns of wall shear stress cause intimal wall thickening (Caro et al., 1969; Ku et al., 1985; Friedman et al., 1981; Igawa et al., 1995; Merickel et al., 1993; Dardik et al., 2005), while increased blood flow and a unidirectional flow environment are associated with vasodilation (Ziegler et al., 1997, 1998; Gnasso et al., 2001; Hutcheson and Griffith, 1991).

It has been shown that the vascular endothelium regulates the arterial wall properties (Kinlay et al., 2001). A uniform shear stress field tends to elongate and align the endothelial cells in the direction of the flow, while low shear stress levels in combination with an oscillatory haemodynamic environment cause irregular shape and the loss of a particular orientation (Davies et al., 2001, 2003; Helmke and Davies, 2002; Nagel et al., 1999; Satcher et al., 1997; Tardy et al., 1997). This morphological variation of the vascular endothelium layer results in different levels of vasoactive substances production like nitric oxide (NO) and endothelin-1 (ET-1) (Noris et al., 1995; Levesque and Nerem, 1985) and consequently

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dissimilar arterial behaviour. Exposure to a relatively low wall shear stress can increase the permeability of the cells, thus increasing the vulnerability of those regions to the atherosclerotic plaque (Okano and Yoshida, 1994). Contrarily, an intense wall shear stress increase causes a rapid cytosceletal remodelling (Nofer et al., 2004; Shyy and Chien, 2002).

The above observations led to a hypothesis that we intend to explore in the present study, i.e. that wall shear stress and near-wall directionality of the flow can trigger the inception of aneurysms and atherogenesis. We developed a computational model to identify high-risk areas for aneurysmal development and atherosclerotic plaque origination. For testing the model, we used an idealized carotid bifurcation geometry, for which the areas where pathologies are most commonly observed are well-documented (Zarins et al., 1983; Giddens et al., 1993; Bossi and Caffarat, 1968; Vega-Basulto et al., 2003). Furthermore, we applied the model on an anatomically accurate, patient-specific fusiform cerebral aneurysm in order to gain insight of where the possibility of the development of a second aneurysm (a "baby" aneurysm) is higher, and where atherosclerotic lesions are more likely to develop.

The model is based on the assumption that the initialization of an aneurysm is connected to reduced local vascular tone, where the pressure force can cause a regional initial ballooning. As far as atherosclerosis is concerned, local stiffening of the artery is assumed (Dardik et al., 2005).

For the present work, we conducted a parametric analysis with various model factors. The model showed an impressive consistency in its prediction of the "Risk Factor" for aneurysm formation and atherosclerosis initiation, and the different parameter values only altered the size of the crucial regions, both for the aneurismal and atherosclerotic cases. For the carotid bifurcation case, the model predictions are consistent with clinical observations.

2. Computational model

The computational model developed attempts to mimic the mechanisms at play and elucidate their relative influence by quantifying the changes of appropriate blood flow parameters. The model uses blood wall shear stress (τ), temporal rate of shear stress change ($\dot{\tau}$), and the vorticity of the flow ($\nabla \times \vec{u}$) as its parameters. The absolute shear stress value is known to play a key role in the EC function. Shear stress levels influence the production of vasoactive substances like NO and ET-1 (Wilkinson et al., 2002; Snow et al., 2001; Ishikawa et al., 1995; Buga et al., 1991; Shiu et al., 2002). High shear stress values cause vasodilation, while low local shear stress values are associated with atherosclerosis.

The oscillatory behaviour of the flow in conjunction with its directionality also influences the biological reaction of the arterial wall. Thus, in the case of strong oscillatory but unidirectional flow fields, vasodilatation is more intense than in the case of steady flow with shear stress levels equal to the average of the oscillatory ones. Conversely, oscillatory flow in combination with a non-unidirectional flow field causes increased stiffening of the artery (Ku et al., 1985; Friedman et al., 1981; Gibson et al., 1993). To incorporate those mechanisms into a model, we employ the rate of shear stress change ($\dot{\tau}$) and flow vorticity ($\nabla \times \vec{u}$) as measures of the oscillatory behaviour and the directionality of the flow, respectively. All those biological reactions are unified under the assumption that vasodilation occurs due to reduced arterial tone while prolonged stiffening of the artery leads to hyperplasia. In the case of atherosclerosis, the

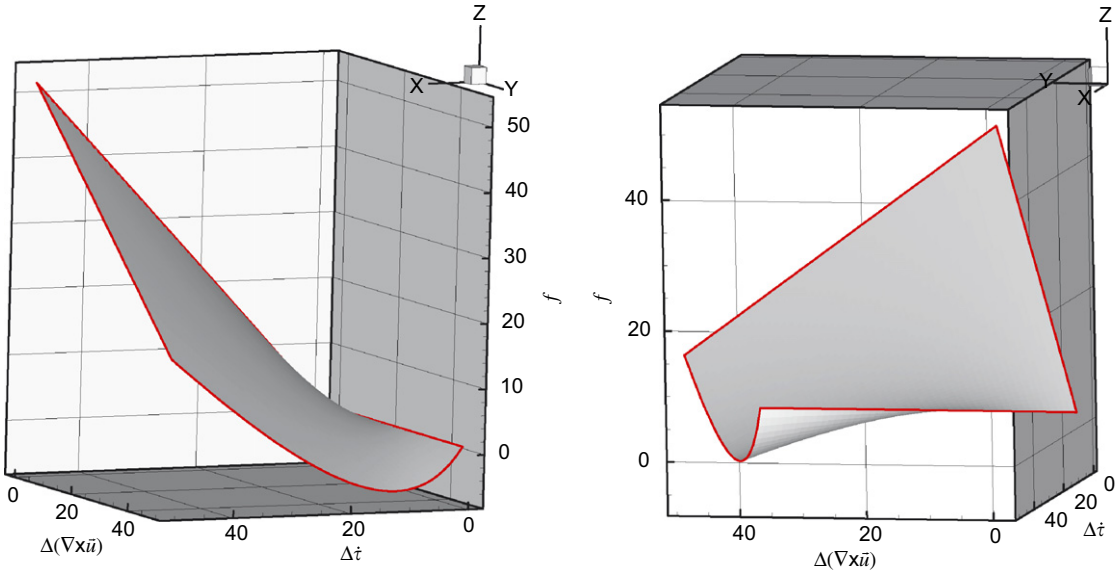

Fig. 1. 3D surface that describes the quantity $f(\Delta\dot{\tau}, \Delta(\nabla \times \vec{u}))$.