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Derivation of flow related risk indices for stenosed left anterior descending coronary arteries with the use of computer simulations

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ABSTRACT

The geometry of the coronary vessel network is believed to play a decisive role in the initiation, progression and outcome of coronary artery disease (CAD) and the occurrence of acute coronary syndromes (ACS). It also determines the flow field in the coronary artery which can be linked to CAD evolution.

In this work geometric 3D models of left anterior descending (LAD) coronary arteries associated with either myocardial infarction (MI) or stable (STA) CAD were constructed. Transient numerical simulations of the flow for each model showed that specific flow patterns develop in different extent in the different groups examined. Recirculation zones, present distal the stenosis in all models, had larger extent and duration in MI cases. For mild stenosis (up to 50%) areas with low time averaged wall shear stress TAWSS (<0.15 Pa) as well as areas with high TAWSS (>3 Pa) appeared only in MI models; in moderate and severe stenosis (>50%) these areas were present in all models but were significantly larger for MI than STA models. These differentiations were expressed via numerical indices based on TAWSS, oscillating shear index (OSI) and relative residence time (RRT). Additionally we introduced the coagulation activation index (CAI), based on the threshold behaviour of coagulation initiation, which exceeded the suggested threshold only for MI models with intermediate stenosis (up to 50%). These results show that numerical simulations of flow can produce arithmetic indices linked with the risk of CAD complications.

1. Introduction

The term coronary artery disease (CAD) describes the formation of atherosclerotic plaques in epicardial coronary arteries. The formed plaques cause the narrowing of the vessel and reduce the blood and oxygen supply to the myocardium. In a significant number of cases CAD leads to complications such as myocardial infarction. These complications are often lethal and make CAD the leading cause or mortality worldwide [1]. Patients diagnosed with CAD receive either pharmacological treatment or coronary revascularization. The choice is based on the severity of the stenosis and the clinical condition of the patient. However several patients receiving pharmacological treatment suffer from complications while at the same time it is possible that other patients take the risk of an unnecessary intervention [2].

While the triggering of thrombus formation is generally considered the rupture of an atherosclerotic plaque, intracoronary ultrasound studies have suggested that plaque rupture itself may not necessarily lead to clinical events [3–5]. Plaque ruptures have been identified in patients with acute coronary syndromes at multiple sites away from the culprit lesion (ACS) [3] and in patients with stable angina or asymptomatic ischemia [4]. Therefore, plaque rupture seems to be a frequent event that requires the contribution of additional factors in order to lead to ACS.

The idea of using quantitative characterization of the coronary geometry and flow conditions as a dynamic risk factor for coronary disease is not novel [6,7]. Several studies on the distribution of atherosclerotic plaques in human arterial systems have shown that atherosclerosis occurs predominantly at certain locations of the vascular tree where the arteries have complex geometry that results in “disturbed” blood flow behaviour [8–11]. Geometry [12] and flow [13] might also be responsible for the thickening of the vessel wall a fact that is considered to predispose to atherogenesis [14]. Statistical correlation between the lesion and the incidence of ACS [15] has also been reported. Flow conditions influence the formation of thrombus via identified mechanisms that act both on the vessel wall and on the biochemical reactions in flowing blood. Mechanical stimulation

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can influence the endothelium cells' response [16,17]; wall shear stress (WSS) can also affect the vulnerability [18], the evolution [19] and even the composition of plaques [20] while mechanical stresses contribute to the rupture of the plaques. Flow directly influences the reactions related to thrombus formation by regulating the transport of involved substances [21]; pathological shear distribution can independently activate the coagulation mechanism [22]; platelet deposition is correlated to flow patterns like flow separation, and recirculation [23,24]. These findings indicate that the thrombogenic potential of a partially blocked coronary artery can be linked to characteristics of the flow field.

As coronary network is located on the heart, it follows the contractions of the heart muscle. This has been simulated in Refs. [25–27] and it has been shown to influence the flow distribution in the bifurcations [27] while it has no significant effect on (computed) time averaged values of WSS [25,27,28]. The rheological behaviour of blood is also complex, as it exhibits shear thinning behaviour for low values of shear rate. However, for coronary flow conditions this is important for lower values of inlet flow rate [29] occurring during a small part of the cardiac cycle [25,30]. So, in most related studies it is modelled as a Newtonian fluid [26,31–36]. For the flow rate in the coronary inlet a number of different approaches have been proposed. 'Average' and widely accepted waveforms for the mass flow and the inlet pressure that can be found in literature [25, 26], obtained from MRI [37] or catheter [38] measurements or animal models [33,34,39], in vitro measurements [26,40]. Simplified pulses with adjusted average mass flow rate have also been used [27,38], as it has been demonstrated that the exact form of the inlet pulse has small influence over the time averaged quantities [38]. The problem of the outlet boundary conditions is more complicated, as the outflow of the main branches of the coronary is mainly determined by the unknown downstream vessel network. In the case of healthy vessel the flow rate in each branch can be defined under the assumption of (almost) constant WSS and Poiseuille flow [25,31]. A more sophisticated approach for the boundary conditions is the use of lumped parameter models analogous to electrical circuits for the inlet/ outlet of the computational domain. These models impose relationships between the pressure and the mass flow and in some cases their time integrals and derivatives at each boundary [41–44].

Existing computational studies on coronary flow have been proved in good agreement with in-vitro experimental results [40]. A number of the published works focus on the effect of different parameters on the results, such as the motion of the vessels [25–27], the existence of bifurcations [45], the off-plane geometry of the coronary and the small alterations of the geometry [40] and the use of non-Newtonian models for blood viscosity [25,29,30]. Other studies apply computational techniques on several problems related to coronary flow that cannot be accessed by experiments or medical examinations, as the study of flow patterns for different types of atheromatic plaques [36], the comparison of different cases of coronary anastomosis [46], pre and post stenting haemodynamics [31,33,47], the effect of foreshortening (deformation) of stents on WSS [34], different methods and types of coronary aneurysm stenting [48] recently computational simulations of blood flow has been used as diagnostic method of stenosis-caused ischemia, via the calculation of the fractional flow reserve [49,50].

We have previously shown that a combination of specific anatomic parameters predispose to vulnerable plaque development, rupture of the plaque and consequent thrombosis [51,52]. In the present study we hypothesized that the different risk for ACS that was statistically attributed to different LAD models can be quantified via specific flow related quantities. These quantities are calculated from the flow field as it is obtained with the use of computational fluid dynamics (CFD) simulations. Finally, using the CFD results we established a set of risk indices appropriate for assessment of an arbitrary case.

2. Materials and methods

2.1. Coronary models

Geometric models of coronary arteries were obtained from previous analyses of patients with an anterior ST-elevation myocardial infarction (MI) and a patent LAD or patients with stable coronary stenoses (STA) and a significant LAD stenosis via coronary angiography [52]. Statistical analysis indicated that coronary stenoses associated with MI were closer to the ostium (inlet) of the LAD compared with stenoses associated with stable CAD. Additionally, in patients with stable CAD the stenosed part of the vessel does not involve bifurcations whereas in MI models there are bifurcations within the stenotic lesion. In our study we used two different groups associated with ACS, MI1 and MI2, according to the statistical analysis [52,53]. The difference between the MI1 and MI2 models is the location of the affected side-branch: in MI1 models it is located upstream the peak of the stenosis while in MI2 models it is located downstream the peak of the stenosis.

Based on these characteristics an 'average' healthy LAD model [52] was constructed, consisting of one main branch and 5 side branches (6 outflows), with total volume $6.922 \times 10^{-7}\,m^3$ and total wall surface $0.0012\,m^2$.

Starting from the healthy LAD geometry the models with maximum stenosis (90%) associated either with MI (MI1 and MI2) or with stable CAD (STA) were constructed (Fig. 1), by introducing a sinusoidal radius reduction as done in previous studies [34,35,54–56]. The geometries with intermediate degrees of stenosis were obtained via linear interpolation.

As mesh independence tests indicated that above 1 million cells the results did not change significantly (~2%) for outlet pressures and WSS, computational grids of about 1.5 million hexahedral cells were created for each geometry, using the Hexa-Block tool of ANSA [57]. 16 different geometries were used for the simulations (Fig. 1), one healthy and 15 with different degrees of stenosis The results for the models with 90% of stenosis were used only to investigate the flow-rates calculated from the boundary conditions.

2.2. Fluid model and boundary flow conditions

Blood was modelled as a Newtonian fluid with the use of the incompressible Navier–Stokes equations, as for LAD dimensions the shear rate is well above the limit where blood exhibits shear-thinning behaviour for almost the whole of the cardiac cycle [25,30,58]. Flow was modelled as laminar (no turbulence model used) as the calculated Reynolds numbers were below 100 even for 90% stenosis. The vessel walls were considered rigid and stationary and no slip boundary condition was imposed for the walls.

Except from the resistance of the coronary arterial network, the movement of the heart muscle is the main determining factor, as the vessels that enter the myocardium are compressed due to contractions. As the structure of the coronary network for each case is inaccessible, the boundary conditions always include some assumptions, and the results are approximate. In this study the method of boundary conditions is based on three main hypotheses: (i) the existence of the stenosis is not changing the aortic pressure or the behaviour of the coronary network downstream the computational domain; (ii) the behaviour of the downstream network can be approximated by a time depended resistance; (iii) WSS(τ_w) for the computational domain of the healthy case is almost constant and approximately 1.5 Pa [16] and flow is approximately Poiseuille [25,31,59].