On the impact of modeling assumptions in subject-specific hemodynamic simulations of low-density lipoproteins transport in aorta

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***Abstract*—In this study we use an image-based hemodynamic model of human aorta to investigate the influence of different strategies of applying boundary conditions (BCs) on low-density lipoproteins (LDL) transport and wall transfer. Findings from simulations clearly show that the imposition of idealized, rather than PC-MRI measured velocity profile as inflow BCs in subject-specific computational models of mass transport could largely affect the location and extension of regions of LDL polarization at the luminal surface of the aorta.**

***Keywords*— Low-density lipoproteins transport, arterial mass transport, computational hemodynamics, atherosclerosis.**

I. INTRODUCTION

THE complex hemodynamics observed in the human aorta make this district a site of election for an in depth investigation of the relationship between fluid structures, transport and patho-physiology. In fact, it is well known that hemodynamics play an important role in the mass transport of blood specimen, and in turn, in their transfer to the vascular wall and ultimately in the localization of vascular disease in areas of complex arterial flow. In particular, the accumulation of lipoproteins in the arterial intima is a hallmark of atherosclerosis. Low-density lipoproteins (LDL) are the most abundant atherogenic lipoproteins in plasma and high plasma levels of LDL are causally related to the development of atherosclerosis [1].

In the last decade the coupling of medical imaging and computational fluid dynamics (CFD) has contributed to enhance the comprehension of the aortic hemodynamics, with the possibility to obtain highly resolved blood flow patterns in anatomically realistic arterial models. In particular, in the context of a subject-specific oriented approach, PC-MRI has emerged as able to provide the anatomical and hemodynamic inputs to even more realistic, fully personalized flow simulations [2]. Moreover, personalized computational modeling of mass transfer has been proposed as a powerful way of addressing abnormalities in mass transfer patterns, which could be in themselves atherogenic [3]. In this regard, a recent study investigated the effects of geometric features of human aorta on the flow pattern and the luminal surface LDL concentration. More in detail, it was investigated the role played by aortic torsion, branching, taper, and curvature on LDL transport and luminal surface distribution in four aortic models with different geometry [4].

In this study we analyze the influence of different possible strategies of applying PC-MRI measured data as inflow boundary conditions (BCs) to confidently model LDL transport and transfer in image-based hemodynamic models of human aorta. In detail, the influence on LDL transport of assumptions regarding the velocity profile at the inlet section of the ascending aorta. We impose PC-MRI measured 3D velocity profiles (i.e. locations-dependent direction and magnitude of velocity vectors at the inlet section) at the inlet of the computational model and compare the obtained results, in terms of low-density lipoproteins transport, to the results of two equivalent computational models with the same instantaneous flow rate prescribed as measured 1D velocity profiles (i.e. magnitude of velocity vectors normal to the inlet surface) and flat velocity profile inlet BCs. Technically, steady-state flow simulations were carried out at three representative phases of the cardiac cycle for the three inlet velocity profiles considered. The LDL distribution at the aortic luminal surface was computed and the results were compared.

The study here presented would contribute to clarify which is the impact of the conditions applied at inflow boundaries on aortic LDL transport. In particular, the comparison of LDL transport at the aortic luminal surface as obtained prescribing idealized *vs* measured velocity profiles as inflow BCs, will contribute to clarify which is the level of detail obtained from measured phase velocity, sufficient to satisfactorily simulate mass transport/transfer in personalized computational hemodynamics models of human aorta.

II. METHODS

The geometry of an ostensibly healthy human aorta was reconstructed from 4D PC-MRI images. PC-MRI slices were used to generate the model of aorta into the Vascular Modeling Toolkit environment by applying a multiple step procedure for the extraction of the surface mesh of the thoracic aorta from PC-MRI data [5]. The finite volume method was applied to perform numerical simulations under steady flow conditions. The general purpose CFD code Fluent (ANSYS Inc., USA) was used on computational mesh-grids with high quality prismatic cells near the wall at the inlet surface and structured tetrahedral elsewhere, semi-automatically generated using ICEM (ANSYS Inc., USA). The domain was equipped with straight flow extensions at the outlet faces and divided into about $4 \cdot 10^6$ cells. Blood was modeled as an isotropic, incompressible, homogeneous, Newtonian viscous fluid with density equal to 1060 kg/m^3 and dynamic viscosity equal to 3.5 cP. The LDL diffusion coefficient in blood was set to $5.94 \cdot 10^{-9}$ m^2/s. Arterial walls

were assumed to be rigid with no-slip condition at the wall. At the outlet sections of the model measured flow rate ratios were imposed as outflow BCs, as detailed in [5].

Steady state LDL transport in flowing blood can be described by the convective-diffusion equation for the LDL concentration *C*:

$$u \cdot \nabla C - D_L \nabla^2 C = 0 \qquad (1)$$

where u is the velocity vector and D_L is the diffusivity of LDL in flowing blood, set to $4.8 \cdot 10^{-12}$ m^2/s [4].

Flow simulations were carried by applying conditions at boundaries as measured at three different phases of the cardiac cycle (i.e. acceleration phase, systolic peak and deceleration phase, Figure 1), for a total number of nine simulations. According to a previous strategy [2], the following BC strategies were applied at the inlet section of the ascending aorta. The first strategy consists in the application of the measured PC MRI velocity profiles at the inlet section. Technically, at the inlet section of the model the measured three components of the velocity were extracted from the phase images. Using phase-contrast flow data, two different inflow conditions were generated, by imposing at the inlet of the ascending aorta: (1) PC-MRI measured 3D velocity profile at systolic peak, and at two phases of the cardiac cycle, one along the acceleration phase and the other along the deceleration phase; (2) PC-MRI measured 1D velocity profile at the same phases of cardiac cycle, obtained considering the measured velocity component orthogonal to the inlet section of the anatomic model (i.e., the axial velocity component). The second strategy is a widely applied approach and consists in the application of the measured velocity waveform at the inlet surface in terms of idealized flat velocity profile, where the velocity magnitude of flat profile was obtained by averaging 1D velocity profile, at each one of the three considered phases of cardiac cycle.

The equation (1), governing mass transport, was solved coupled to the Navier-Stokes equations by imposing the following BCs:

$$\text{BC } \textit{inlet}: \quad C = C_0 \qquad (2)$$

$$\text{BC } \textit{outlet}: \quad C = \frac{\partial C}{\partial n} \qquad (3)$$

$$\text{BC } \textit{wall}: \quad D_L \left(\frac{\partial C}{\partial n}\right) = v_w C_w \qquad (4)$$

where C_0 is the LDL concentration in the bulk flow (set equal to $2.86 \cdot 10^{-9}$ mol/m^3 [4]), C_w is the concentration of LDLs at the luminal surface of the artery, v_w is the filtration velocity of fluid across the vessel wall (set equal to $4 \cdot 10^{-8}$ m/s [4]), and suffice *n* indicates the direction normal to the boundary.

LDL transport was computed for the three inflow conditions cases and the impact of the choice of idealized rather than measured velocity profiles as inflow BCs was investigated focusing on LDL transfer to the aortic luminal surface.

III. Results

As main finding of the study the uptake of LDL at the aortic wall (normalized with respect to the initial LDL concentration C_0 at the aortic inlet section) is reported. In detail Figure 1 presents the LDL accumulation profiles at the luminal surface obtained by imposing in silico (FLAT panel) and in vivo (1D and 3D panels) velocity profiles as inflow BCs for the three simulated phases of the cardiac cycle. Notably, differences in LDL patterns at the luminal surface are present, depending on the applied velocity profile at the inflow. In detail, the surface area subjected to elevated LDL accumulation is markedly wider than the 3D and 1D cases, when flat velocity profile is prescribed at the aortic inflow section. The FLAT case presents three luminal regions at the aortic arch subjected to severe polarization of LDL, more evident during the acceleration phase of the cardiac cycle (inner lateral edge of the brachiocephalic artery, intrados of the ascending aorta and inner wall of the descending aorta). The same regions were identified in [4], as interested by elevated LDL accumulation. LDL polarization at these luminal regions sensibly decreases in 1D and 3D simulation cases. Results obtained for 3D and 1D cases show a more uniform LDL distribution at the wall along the aortic arch, with a weak increase in LDL polarization at the inner wall of the descending aorta. In general, Figure 1 confirms that light or negligible differences can be appreciated in LDL transport between 1D and 3D cases at the three cardiac phases here investigated.

IV. Conclusion

The findings of this study show that the imposition of idealized velocity profile as inlet BCs in subject-specific computational hemodynamics models of mass transport in the human aorta could largely affect the location and extension of regions of LDL polarization at the luminal surface. We conclude that the plausibility of the assumption of idealized velocity profiles as inlet BCs in personalized model of the aortic hemodynamics could not, or could loosely, hold true. This finding needs further investigation, because of the fact that it is derived from steady-state flow analysis. The same analysis will be extended to unsteady-state simulations, applying the same scheme as proposed in previous works [2]. Ultimately, the approach here proposed is intended to be applied to elucidate the role played by the aortic helical flow in mass transport [6], in particular in testing the hypothesis that the promoted-by-helicity mixing of blood could be beneficial in suppressing severe LDL polarization at peculiar aortic regions, thus being part of the physiologic atheroprotective mechanism.

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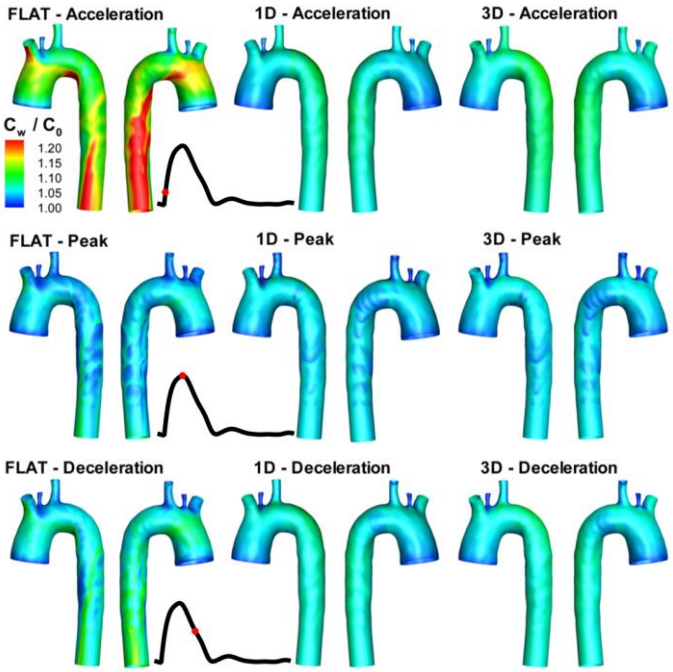

Fig. 1. Comparison of the normalized LDLs concentrations at the luminal surface for the simulated inflow boundary conditions.