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A rational approach to defining principal axes of multidirectional wall shear stress in realistic vascular geometries, with application to the study of the influence of helical flow on wall shear stress directionality in aorta

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ABSTRACT

The distribution of arterial lesions is attributed by the prevalent mechanistic theory to the proatherogenic role played by low and oscillatory wall shear stress (**WSS**). However, discrepancies observed when comparing **WSS** distribution with location of regions with lesion prevalence challenge this theory and have recently stimulated the idea that a role in endothelial mechanosensing is played by **WSS** multidirectionality, which could contribute to explain the observed discrepancies.

Here an approach is presented for analyzing the multidirectional nature of **WSS** in complex vascular geometries. Using an essential geometric attribute of the vessel (its centerline), the local **WSS** vector is projected along an “axial” direction (aligned with the tangent to the vessel's centerline), and “secondary” direction (orthogonal to centerline's tangent), which is related to secondary flow. The **WSS** projection scheme is applied: (1) to a realistic computational hemodynamic model of human aorta, with the aim to come up with a plausibility checking regarding its consistency; and (2) to investigate if an aortic hemodynamics characterized by different amount and topology of helical flow (HF) could influence **WSS** directionality.

The projection scheme confirmed its consistency and plausibility in realistic arterial geometries and allowed to get insight into the relationship between aortic intravascular fluid structures and **WSS** directionality. The findings of this study clearly show the potential of the projection scheme as quantitative tool for an in depth investigation of the **WSS** multidirectional nature. The proposed approach enriches the arsenal of tools available to study and exploit the role played by local hemodynamics in vascular disease.

1. Introduction

There is clear evidence that hemodynamics plays a critical role in vascular disease. The non-uniform distribution of atherosclerotic lesions within arteries has been attributed to the proatherogenic role played by low and oscillatory wall shear stress (**WSS**) on endothelial cells (ECs). This theory, which underlies most current research concerning localizing factors of vascular disease (Mohamied et al., 2015), results from the combination of the observations that (1) disease is promoted by low **WSS** (Caro et al., 1971) and (2) lesions occur in luminal regions where **WSS** direction is oscillatory (Ku et al., 1985).

However, the discrepancies observed when comparing distribution of low/oscillatory **WSS** with location of regions with lesion prevalence challenge this theory, which does not fully account for **WSS** multidirectionality along the cardiac cycle (Peiffer et al., 2013a, 2013b, 2013c; Mohamied et al., 2015).

Recent findings on EC sensing of flow direction could explain (some of) these discrepancies (Mohamied et al., 2015). In this regard: (1) there is evidence for a relation between flow directionality and ECs mechanotransduction pathway (Martorell et al.,

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2014); (2) ECs response depends on the multidirectional nature of **WSS** (Wang et al., 2012), whose direction can alter the balance of protective and inflammatory stimuli to cells (Wang et al., 2013); (3) a relation between flow directionality and disease was recently provided characterizing disturbed shear as the average magnitude of **WSS** component acting perpendicular to the local direction of the cycle-averaged **WSS** (Peiffer et al., 2013a; Mohamied et al., 2015).

All these findings confirm that the relation between flow directionality and disease in arteries is still not clarified.

Stimulated by these still open questions, here an approach for analyzing the multidirectional nature of **WSS** is presented. In detail, a strategy is proposed driven by topological features of the vasculature and inspired by biofluid mechanics paradigms (Alastruey et al., 2012), demonstrated for idealized geometries and here extrapolated for the study of real vascular geometries. Based on this strategy, the **WSS** vector is projected along two directions, here identified with the direction tangent to vessel's centerline (i.e., the “preferential direction” for the flow is along the streamwise axis of the vessel) and with the direction related to secondary flow.

The topology-driven projection strategy, which in trivial flows is equivalent to the one proposed by Peiffer et al. (2013a), could be an helpful tool of investigation in complex flows.

The **WSS** projection scheme is here applied to an image-based computational hemodynamics model of human aorta, to check its consistency in a first step.

Secondly, stimulated by the recognized physiological significance of helical flow (HF) in the arterial system (Liu et al., 2015), we evaluated the effectiveness of the proposed **WSS** projection scheme to investigate whether different amount and topology of aortic helical flow (HF) could influence **WSS** directionality and, ultimately, disturbed shear. The analysis corroborates the convincement that the proposed scheme could be effective in the investigation of the **WSS** multidirectional nature.

2. Materials and methods

4D phase contrast magnetic resonance imaging (PC-MRI) images of an ostensibly healthy human aorta were acquired as described in previous studies (Morbiducci et al., 2011; Tresoldi et al., 2014). PC-MRI images were used to generate the geometric model of aorta (Fig. 1) into the Vascular Modeling Toolkit (VMTK) environment (Antiga et al., 2008) and to extract boundary conditions (BCs), as described in Gallo et al. (2012a) and Morbiducci et al. (2013). The finite volume method was adopted to solve the governing equations of the fluid motion under unsteady flow conditions. The general purpose CFD code Fluent (ANSYS Inc., USA) was used on a tetrahedral computational mesh-grid of cardinality 4,800,000. Arterial walls were assumed to be rigid. At the outlet sections of the supra-aortic vessels the measured flow rates were prescribed as outflow (Gallo et al. 2012a; Morbiducci et al., 2013). The applied inflow BCs strategy is described below. A detailed description of the applied computational scheme can be found in Morbiducci et al. (2013).

2.1. Multidirectional WSS description in real vascular geometries

To analyze the multidirectional nature of **WSS** in complex vascular geometries, a method is proposed which use an essential geometric attribute of the vessel, its centerline. Locally, the **WSS** vector is projected along (1) the “axial direction”, here intended as the direction aligned with the tangent to vessel's centerline, and (2) the secondary direction, orthogonal to the axial direction and related to secondary flow (Fig. 1).

In order to perform **WSS** projection, centerlines of vascular segments are extracted in the form of set of discrete points in space (computed as the centers of maximal spheres inscribed in the vessel lumen) using VMTK. For the obtainment of reliable **WSS** projection, the discrete and noisy observations of the 3D curve **C** representing the centerline, could be not sufficient because of the need for calculating the derivative of centerline **C** at each curvilinear abscissa S. To obtain an analytical, continuous formulation describing the centerline and its derivatives as curves in the space, the 3D free-knots regression splines were selected as a basis of representation for **C** and its derivatives. Here a scheme, as previously proposed for arterial centerlines characterization (Sangalli et al., 2009; Gallo et al., 2015), was applied.

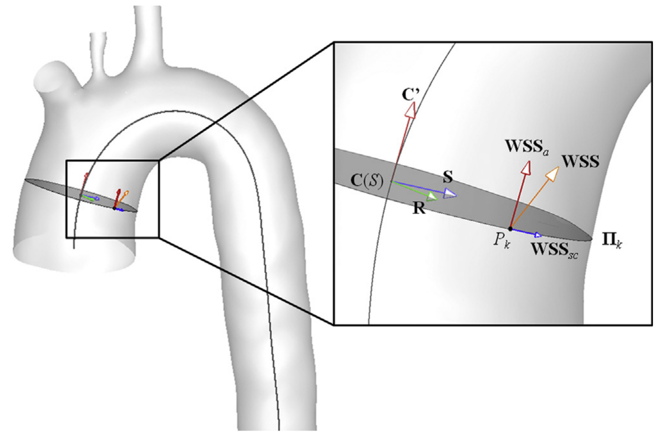

Fig. 1. Projection of the local **WSS** vector at the generic point P_k at the vessel wall (1) along the axial direction, $\mathbf{WSS}_{ax}$, related to the tangent to the vessel's centerline and (2) the secondary direction, $\mathbf{WSS}_{sc}$, related to secondary flow on plane Π_k (orthogonal to the centerline) point P_k belongs to.

The obtainment of analytical expressions for vasculature centerline, allows for projection of the local **WSS** vector along the axial and secondary direction. As first step, the cross-section, orthogonal to centerline **C**, to which the generic point P_k (x_k, y_k, z_k) at the vessel wall belongs (Fig. 1) is identified through the minimization of the functional Ψ

$$\Psi = \frac{|\mathbf{R}(S)\cdot\mathbf{C}'(S)|}{|\mathbf{R}(S)||\mathbf{C}'(S)|} \tag{1}$$

where **R** is the vector identified by point P_k at the luminal surface and a generic point of curvilinear abscissa S on the centerline and **C'** is the vector tangent to the centerline at curvilinear abscissa S (Fig. 1). It is clear from Eq. (1) that: (1) Ψ is the internal product of the vector tangent to the centerline at a certain curvilinear abscissa (the point of application) and the vector from point on the centerline and point P_k; (2) the minimization of Ψ, moving along the centerline, allows to identify both the direction of vector **C'** orthogonal to vector **R** and its point of application along the centreline (i.e. the plane Π_k, orthogonal to the centerline, to which point P_k belongs). In this way, it is possible to unambiguously identify the vessel cross-section to which each point P_k at the luminal surface belongs (Fig. 1). This process, which is straightforward for straight cylindrical conduits, is not trivial when applied to realistic vascular geometries characterized by sudden lumen expansion/reduction, torsion, tortuosity, not circular cross-sections, branching and bifurcations.

After all the points at the luminal surface have been associated to the vessel cross section they belong to, we define as axial **WSS** at point P_k, the projection of vector **WSS** along the direction of the tangent to the centerline **C'** at the curvilinear abscissa S_k (Fig. 1)

$$\mathbf{WSS}_{ax} = \frac{\mathbf{WSS}\cdot\mathbf{C}}{|\mathbf{C}|}\frac{\mathbf{C}}{|\mathbf{C}|} \tag{2}$$

The secondary component can be obtained as the projection of **WSS** vector along the direction of vector **S**

$$\mathbf{WSS}_{sc} = \frac{\mathbf{WSS}\cdot\mathbf{S}}{|\mathbf{S}|}\frac{\mathbf{S}}{|\mathbf{S}|}\mathbf{S} = \frac{\mathbf{C}\times\mathbf{R}}{|\mathbf{C}||\mathbf{R}|} \tag{3}$$

where **S** is given by the external product of **C'** and of vector **R**, directed from the point of application on the centerline (curvilinear abscissa S_k) to point P_k (Fig. 1):

2.2. Aortic helical flow

Here, findings from a previous study were used, where the aortic flow was subjected to characterization in terms of HF content and topology (Morbiducci et al., 2013). Remembering that helicity $H(t)$ in a fluid flow confined to a volumetric domain D can be expressed as (Moffatt and Tsinober, 1992)

$$H(t) = \int_D \mathbf{v}\cdot\boldsymbol{\omega}\, dV \tag{4}$$

where **v** and **ω** are the velocity and vorticity vectors, in Morbiducci et al. (2013) helicity-based descriptors were applied for a quantitative analysis of HF patterns in the hemodynamic model of Fig. 1. In particular, we observed, also by using the quantity local normalized helicity (LNH, a measure of the angle between velocity and vorticity vectors)

$$\mathrm{LNH} = \frac{\mathbf{v}\cdot\boldsymbol{\omega}}{|\mathbf{v}|\,|\boldsymbol{\omega}|} \tag{5}$$