Wall shear stress in normal left coronary artery tree

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Abstract

Despite the fact that the role of wall shear stress (WSS) as a local mechanical factor in atherogenesis is well established, its distribution over the entire normal human left coronary artery (LCA) tree has not yet been studied. A three-dimensional computer generated model of the epicardial LCA tree, based on averaged human data set extracted from angiographies, was adopted for finite-element analysis of the Navier–Stokes flow equations treating blood as non-Newtonian fluid. The LCA tree includes the left main coronary artery (LMCA), the left anterior descending (LAD), the left circumflex artery (LCxA) and their major branches. In proximal LCA tree regions where atherosclerosis frequently occurs, low WSS appears. Low WSS regions occur at bifurcations in regions opposite the flow dividers, which are anatomic sites predisposed for atherosclerotic development. On the LMCA bifurcation, at regions opposite to the flow divider, dominant low WSS values occur ranging from 0.75 to 2.25 N/m². High WSS values are encountered at all flow dividers. This work determines, probably for the first time, the topography of the WSS in the entire normal human LCA epicardial tree. It is also the first work determining the spatial WSS differentiation between proximal and distal normal human LCA parts. The haemodynamic analysis of the entire epicardial LCA tree further verifies the implications of the WSS in atherosclerosis mechanisms.

Keywords: Wall shear stress; Atherosclerosis; Coronary artery disease

1. Introduction

Atherosclerosis shows a predilection in regions of arterial tree with haemodynamic particularities (Glagov et al., 1988), as local disturbances of wall shear stress (WSS) in space (Sabbah, et al., 1986), local high concentrations of lipoproteins (Fatourae et al., 1998) as well as local velocity and viscosity disturbances (Giannoglou et al., 2002) and morphological (geometrical) particularities, as bends, bifurcations, trifurcations.

There are numerous references supporting the widely known physicians finding that lesions are more frequent in the proximal portions of the three major coronary arteries and are considerably less prominent in the distal arteries and their branches (Enos et al., 1953; Halon et al., 1983). In these studies the prevalence of atherosclerosis in the two major branches of the left coronary artery (LCA) was analyzed. In particular, there was a clustering of lesions in the left anterior descending (LAD) immediately after the first diagonal branch and in the origin of the first diagonal branch. As far as the left circumflex artery (LCxA) is concerned, it was significantly more frequent involvement around the origin of the first marginal branch. As Enos et al. (1953) noticed in their landmark article, regarding the US casualties in Korea, the importance of the bifurcation pattern is dominant regarding its implication to atherosclerosis. According to their observations, the lesions are commonly located at or near points of bifurcation. A negative correlation was found between intimal thickness and WSS. On the contrary, high value
of the WSS seems to inhibit intimal thickening (Friedman et al., 1983).

Early works in the coronary arteries describe the experimental topography of atherosclerosis (Montenegro and Eggen, 1968; Halon et al., 1983; Enos et al., 1953; Velican and Velican, 1980; Fox et al., 1982). These pathological data permit us to attempt a preliminary research work relating the computational results of blood flow in the previously reported LCA tree model (Dodge et al., 1988, 1992) to the atherosclerosis localization. In the past years, numerous computational fluid dynamics analyses were performed for various human coronary artery segments. With the advancements made in computer hardware–software, it is now reasonable to expand the numerical solutions so as to include numerous branches and nearly the whole coronary tree (Dodge et al., 1988, 1992).

The purpose of our study was to numerically analyze the WSS distribution (topography) over the normal human LCA tree. Main emphasis is put on the:

(a) distribution of the WSS on the normal human LCA tree, particularly at the bifurcations,
(b) distribution differentiation of the WSS values between proximal and distal LCA parts as well as on the,
(c) contribution of the low WSS in relation to the localization of atherosclerotic lesions in the LCA tree.

Using the LCA tree finite-element analysis we demonstrate that there are marked local differences in the magnitude of WSS values at bifurcations as well as in the magnitude of WSS values between proximal and distal LCA tree regions. To the best of our knowledge, there is no published computational work determining the topography of the WSS in the normal human LCA tree. Furthermore, there is no work determining the spatial differentiation of the WSS between proximal and distal LCA parts.

2. Material and methods

2.1. Geometry

Experimental measurements of the intrathoracic spatial location of specified coronary segments on the normal human heart were previously reported (Dodge et al., 1988, 1992). These studies (Dodge et al., 1988, 1992) were based on 83 angiographies taken from normal subjects. The intrathoracic location and course of each one of the 23 arterial segments and branches, which are commonly used by the physician to describe the localization of coronary disease, were reported. All data were processed with a Computing Aided Design (CAD) program, resulting in a three-dimensional geometry model of the LCA tree. Angiographic data used for geometry construction correspond to end-diastole. Thus doing, one avoids variance attributable to motion during cardiac cycle. Therefore, there was no motion incorporated in the CFD calculations. This model included the left main coronary artery (LMCA), the LAD, the LCxA and their main branches: the first obtuse marginal (OM1), the second obtuse marginal (OM2), the first septal (S1), the first diagonal (D1), the second septal (S2), the second diagonal (D2), the third septal (S3) and the third diagonal (D3) branch. Fig. 1 shows the geometry of the LCA tree, as it was above described.

Data describe the vessel centerline location (polar coordinates) and vessel diameter at each segment. In particular, the vessel centerline was constructed using

(a) radius,
(b) azimuth angle between projection of radius onto transverse plane and anterior–posterior axis and
(c) angle between radius and transverse plane.

Once the vessel centerline construction was completed, the appropriate vessel diameter was applied at each segment, and the final vessel geometry was acquired via a computerized extrusion process of the pre-processing CAD program. These data were proven to be good enough to describe the anatomic location of the various anatomical segments and the final geometry was found to be satisfactory as a model simulating the normal human left coronary anatomy.
The lumen diameter of the LMCA orifice measured 4.5 mm, while the corresponding values of the LAD and LCx measured 3.7 and 3.4 mm, respectively. The outlet LAD diameter at the apex of the heart was of 0.9 mm, while the corresponding diameter of the LCx at the outlet was of 1.3 mm. For the first, second and third diagonal the corresponding diameters were of 1.1, 1.0 and 0.9 mm, respectively, while the first, second and third septal diameters were of 0.9, 0.7 and 0.7 mm, respectively. For the LCx branches, the outlet diameters of the first and second obtuse marginal were of 1.1 and 1.0 mm.

2.2. Computational grid

All geometrical data were input into a specialized pre-processing program for grid generation. In total, 44,452 grid nodes were utilized giving rise to 196,902 computational tetrahedral. Figs. 2 and 3 show details of the utilized non-structured grid of the human LCA tree. Fig. 4 shows the distribution of computational grid nodes of the LAD vessel in a cross-sectional area located in a region close to the origin of the second septal branch. Note the dense grid node distribution, for adequate depiction of physical blood quantities, near the perimeter (endothelium) region. The relative error in the velocity components and in the haemodynamic parameter of WSS was computed and used as a quantitative measure of the effect of grid density. The used mesh was based on the computational results of mesh-independence studies. The number of nodes used to define the mesh independence increased initially to 59,524 nodes and at a later stage to 80,889 nodes. The relative error in the derived haemodynamic parameter of WSS was calculated and used as a quantitative measure of the grid density effects upon the results.

2.3. Flow equations, boundary flow conditions, and solution

The blood velocity is assumed to be uniform at the orifice of LMCA. The applied inflow conditions mimic typical coronary blood flow velocity, 0.17 m/s, under resting conditions. Moreover, flow discharges were set analogous to the third power of the branching vessel diameter according to Murray’s law (Murray, 1926).
respectively (Sharma and Bhat, 1992). The components (K) are local temperature and reference temperature, changes (maximum 6%) (Santamarina et al., 1998).

To 1 Hz frequency, only slightly affects the velocity impermeable material. Coronary arteries movement, up it while the arterial wall is comprised of non-elastic and laminar, isothermal, with no external forces applied on... 

Table 1 shows the values of the outflow discharges as a percentage of the inlet flow.

All computational grid data, as well as all physical flow data determined from the boundary conditions, were imported into the main Computational Fluid Dynamics solver (Fluent release 5.5, FLUENT Inc., Kelkar and Patankar, 1988). The numerical code, which was previously validated (Kelkar, 1989), solves the governing Navier–Stokes flow equations. In the generality, these equations solve the mass, momenta and energy conservation. The assumptions made about the nature of the flow are that it is three-dimensional, steady, laminar, isothermal, with no external forces applied on it while the arterial wall is comprised of non-elastic and impermeable material. Coronary arteries movement, up to 1 Hz frequency, only slightly affects the velocity... 

The WSS contour values increase from proximal to distal LAD parts. Contour plots of the WSS magnitude distribution at the LCxA are shown in Fig. 8. Low dominant values range from 1.41 to 4.05 N/m². Note that the WSS values rapidly increase in the OM1 vessel. Similar behavior exhibits the OM2 branch.

The WSS contour values increase from proximal to distal LAD parts, shown in Fig. 9. The dominant WSS values immediately downstream to the D3 and S3 are of the order of 8.75 N/m². These values increase further downstream.

Fig. 10 shows the contours of the WSS magnitude distribution at the origin of the D1–S1 and D2–S2 branches. At the origin of these branches, at regions opposite to the flow dividers, the WSS exhibit low values. Furthermore, these values increase from D1–S1 to D2–S2 segments. At the D3–S3 branch, the low dominant WSS values range from 5.82 to 7.04 N/m².

### Table 1

<table>
<thead>
<tr>
<th>LCxA</th>
<th>OM1</th>
<th>OM2</th>
<th>S1</th>
<th>D1</th>
<th>S2</th>
<th>D2</th>
<th>S3</th>
<th>D3</th>
<th>LAD(distal)</th>
</tr>
</thead>
<tbody>
<tr>
<td>22.44</td>
<td>5.82</td>
<td>15.42</td>
<td>2.00</td>
<td>5.49</td>
<td>1.40</td>
<td>4.72</td>
<td>3.21</td>
<td>4.20</td>
<td>35.27</td>
</tr>
</tbody>
</table>

The WSS contour values now range from 1.04 to 2.64 N/m². Finally, Fig. 7 (third view) shows the proximal LAD branch with S1, D1 and OM1 segments. Note that the WSS values increase from proximal to distal LAD parts. The WSS contour values increase from proximal to distal LAD parts, shown in Fig. 9. The dominant WSS values immediately downstream to the D3 and S3 are of the order of 8.75 N/m². These values increase further downstream.

### 3. Results

All spatial WSS values are shown in filled contours coupled with iso-contour line form. These contours show the WSS magnitude and not its spatial direction. Contour labels appear in figures, range from 1 to 15, and correspond to the 15 color levels also shown in figures. The results indicate that on the LMCA bifurcation, at regions opposite to the flow divider, dominant low WSS values occur, ranging from 0.75 to 2.25 N/m² (contour numbers 1–5), Fig. 5 (first view). Low WSS values occur at regions opposite to the flow divider at either LMCA, or proximal LAD or LCxA branches. High curvature affects the velocity distribution at the flow divider, giving rise to high WSS values. Fig. 6 shows (second view) the dominant low WSS contour values on the LMCA bifurcation. This contour values distribution is viewed from an angle diametrically opposite to the one shown in Fig. 5. Dominant low WSS contour values now range from 1.04 to 2.64 N/m². Finally, Fig. 7 (third view) shows the proximal LAD branch with S1, D1 and OM1 segments. Note that the WSS values increase from proximal to distal LAD parts. Note the WSS values rapidly increase in the OM1 vessel. Similar behavior exhibits the OM2 branch.

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Fig. 5. Contour plots of the WSS (N/m²) magnitude distribution at the LMCA bifurcation (first view). Emphasis is put on low WSS contour values.

Fig. 6. Contour plots of the WSS (N/m²) magnitude distribution at the LMCA–LCxA bifurcation (second view).

Fig. 7. Contour plots of the WSS (N/m²) magnitude distribution at the proximal LAD branch (third view).

Fig. 8. Contour plots of the WSS (N/m²) magnitude distribution at the LCxA.

Fig. 9. Contour plots of the WSS (N/m²) magnitude distribution at distal LAD branch.

Fig. 10. Contour plots of the WSS (N/m²) magnitude distribution at the origin of the D1, S1, D2, S2 and OM1 branches.
Finally, Fig. 12 shows WSS (N/m²) colored vectors at the LMCA–LCxA bifurcation. Detailed results of the WSS were obtained at the bifurcation regions: (a) LMCA, (b) OM1, (c) OM2, (d) D1–S1, (e) D2–S2, and (f) D3–S3. The amount of utilized grid nodes range between 6000 and 13 000, depending upon the physical size of the lumen as well as upon the WSS gradient. The computed average WSS at the LMCA is found to be $3.93 \pm 0.01 \text{N/m}^2$, at OM1 $6.45 \pm 0.05 \text{N/m}^2$, at OM2 $7.24 \pm 0.03 \text{N/m}^2$, at D1–S1 $6.30 \pm 0.01 \text{N/m}^2$, at D2–S2 $7.21 \pm 0.01 \text{N/m}^2$ and finally at D3–S3 $10.72 \pm 0.07 \text{N/m}^2$ ($p < 0.001$ for all above cases).

4. Discussion

In the last few years a number of papers have been published dealing with computational analysis and distribution of the WSS in the human coronary arteries (Giannoglou et al., 2000, 2002; Gibson et al., 1993; Krams et al., 1997). Most of these research works were concentrated on particular regions of the coronary tree. WSS is determined from velocity gradients. Any non-zero value of the WSS denotes a non-uniform haemodynamic environment. In case of LMCA bifurcation, shown in Figs. 5 and 6, high WSS values tend to form a “ring” located at the origin of the LCxA. High WSS values occur at the “cervix” (proximal region) of the origin and at the flow divider (distal region). At the “hips” of the LMCA bifurcation, i.e. at regions opposite the flow divider, located at the outer walls of LAD and LCxA, low WSS values occur. At all LCA tree bifurcations, the WSS distribution reveals regions of high values occurring at the associated “rings”, in the vicinity of the flow dividers. Low WSS value regions are located at the sidewalls opposite to the flow divider as it is evident from all figures shown. Fig. 12 shows the WSS magnitude and direction at the LMCA–LCxA bifurcation. The distribution is in accordance with the localization of atherosclerotic lesions in this area (Svindland, 1983; Grottum et al., 1983). Thus, there is strong evidence that low WSS values are possibly correlated to the localization of atherosclerotic lesions.

The WSS exhibits high values in the distal regions of the LCA, see Fig. 9, where the magnitude of the mean flow velocity is relatively higher, probably due to vessel tapering. However, because of the lack of existence in the model of very small vessels that penetrate the myocardium, the WSS results are, probably, artificially high. The low WSS values distribution is in accordance with the frequent localization of atherosclerotic lesion in the proximal LCA regions and it is documented from numerous pathological studies (Montenegro and Eggen, 1968; Halon et al., 1983; Enos et al., 1953; Velican and Velican, 1980; Fox et al., 1982). The strong correlation between averaged low WSS and the localization of atherosclerotic lesions in arterial bifurcations is known (Glagov et al., 1988; Asakura and Karino, 1990). In case of the LAD, the atheroma shows a high prevalence immediately after the first diagonal branch and at the origin of the branch. Similarly, in the LCxA there is a predilection for obstructive lesions in and around the origin of the first marginal branch.

It has also been proved that endothelial cells are subject to morphological alterations, which are activated not only via changes of wall shear stress magnitude but also from its orientation (Levesque et al., 1986; Flaherty et al., 1972; Reidy and Bowyer, 1977). Elongation of the endothelial cells occurs in regions of high WSS, having the longest cell axis oriented parallel to the flow direction (Davies and Tripathi, 1993). Conversely, in low WSS regions, endothelial cells of polygonal shape occur. These cells are not oriented to any direction. It is possible for these
local alterations in endothelial cell morphology to yield different size permeability for the various blood constituents. Therefore, endothelial cells from regions subjected to various values of WSS exhibit various biological and biochemical functions (Reidy and Bower, 1977). It seems that cell surface as well as subcellular distribution of shear stress plays a key role in pathogenesis of atherosclerosis (Skarlatos and Hollis, 1987; Gimbrone et al., 2000; Honda et al., 2001; Flaherty et al., 1972; Urbich et al., 2000). Endothelial cells discriminate between subtle variations in temporal and spatial shear stress. Thus, cellular structures probably serve as mechano-transductions (Barbee, 2002). Sensitization for the WSS signaling pathway may be initiated under specific blood flow disturbances. Probably, multiple pathway signal transduction, concerning additional mechanical factors, are involved in atherogenesis. Endothelial cells can discriminate these blood flow originated stimuli and transduce them into genetic regulatory events via certain promoters of biomechanically inducible genes. Certain genes support an atheroprotective role, but some others play an atherogenic role favoring lesion formation and progression, depending on the particular hemodynamic conditions. Henceforth, genes favoring atherogenesis may be stimulated from the presence of flow disturbances. However, full three-dimensional structural analysis, in combination with applied experimental measurements, is needed to better establish, on cellular level, the exact role of mechanical factors in atherogenesis.

The assumption of flat entrance velocity profile affects, to a certain degree, the WSS results in the LMCA and in the proximal regions of the LAD and LCxA. However, further downstream this flat velocity profile has little or no effect on the WSS calculation. Spatial and temporal WSS appear to be significant factors regulating the endothelial cell biology. Potential interplay between these two components of WSS should be further investigated. The performed flow analysis is based on the steady flow assumption, while the utilized velocity value at the vessel orifice corresponds to the peak of diastole. Therefore, the results refer to the maximum velocity throughout the LCA tree. Arterial movement has to be taken into account since the applied acceleration force will yield a different flow field. It is expected that the flow pattern will be seriously altered, particularly at distal LCA tree regions. Furthermore, near future work should take into account additional outflow discharges through smaller branches, at distal LCA tree regions, that feed the myocardium. These discharges reduce the outflow at the LAD exit boundary of the model, offsetting the effect of taper, thus yielding smaller WSS values than those presented.

Current analysis was performed using the flow discharge to be analogous to the third power of the branching vessel diameter according to Murray's law (Murray, 1926). However, to further investigate the effects of the flow discharges, additional numerical analysis was performed. In this case, the flow discharges were set analogous to the second power of the branching vessel diameter. Results indicate that although the absolute values of the physical quantities vary, the general flow pattern and most importantly the conclusion derived remains unaltered.

5. Conclusion

The topography of WSS in the entire normal human epicardial three-dimensional tree of the LCA was determined under resting flow conditions. The computational model showed a marked difference in both the magnitude and spatial distribution of WSS values everywhere in the LCA tree. This study showed that low WSS regions occur at bifurcations in regions opposite the flow dividers, which are anatomic locations predisposed for atherosclerotic development. Low WSS values appear in the proximal regions of the LCA tree, where atherosclerosis frequently occurs. Results indicate that on the LMCA bifurcation the dominant low WSS values range from 0.75 to 2.25 N/m².

References


