Hemodynamic impacts of various types of stenosis in the left coronary artery bifurcation: A patient-specific analysis

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Abstract

This study investigates the hemodynamic changes to various types of coronary stenosis in the left coronary artery bifurcation, based on a patient-specific analysis. Twenty two patients with left coronary artery disease were included in this study. All stenoses involving the left coronary artery bifurcation were classified into four types, according to their locations: A) left circumflex (LCx) and left anterior descending (LAD), B) LCx only, C) left main stem only, and D) LAD only. Computational fluid dynamics (CFD) was performed to analyze the flow and wall shear stress (WSS) changes in all reconstructed left coronary geometries. Our results showed that the flow velocity and WSS were significantly increased at stenotic locations. High WSS was found at >70% lumen stenosis, which ranged from 2.5 Pa to 3.5 Pa. This study demonstrates that in patients with more than 50% stenosis in the left coronary artery bifurcation, WSS plays an important role in providing information about the extent of coronary atherosclerosis in the left coronary artery branch.

Keywords: Atherosclerosis, coronary artery disease, hemodynamics, wall shear stress
Hemodynamic parameters cannot be directly measured in vivo; accordingly, computational fluid dynamic analysis has become established as a method to predict hemodynamically induced shear stress in the coronary arteries. Low shear stress normally occurs at the bifurcated region due to the coronary angulation [1]. Recently, wide angled bifurcations have been reported to lead to the development of atherosclerosis [2]. Studies using medical imaging techniques have revealed the distribution of coronary stenosis in the left main bifurcation, and evaluated the relationship between the bifurcation angle and development of coronary disease [3,4]. It is generally believed that the left coronary artery geometry is more complicated than the right coronary artery since the left side consists of two large main branches forming an angle, with many side-branches [2, 5, 6]. The bifurcation stenosis has been classified and identification of the appropriate classification is a significant component in planning the appropriate treatment [7]. A stenosis of greater than 50% diameter results in significant flow changes to the coronary artery [8].

Early studies used computational fluid dynamics to analyze a >50% coronary stenosis distributed around the main bifurcation with promising results achieved [9-11]. Results showed the change of flow parameters at the bifurcated regions, with some effects on the hemodynamic factors in coronary side-branches. Recent studies investigated the coronary blood flow under normal and diseased condition, with an assumed degree of stenosis [12,13]. Despite the use of computer simulation in these studies to investigate the hemodynamic changes in coronary models, there have been no reports about the realistic bifurcation stenosis based on patient-specific models. In this study, we aim to investigate
the hemodynamic patterns and wall shear stress with detection and classification of the
types of bifurcation stenosis based on a group of patients with suspected coronary artery
disease (CAD). Research findings from this study could improve our understanding of
hemodynamic effects of various stenosis distributions in the left coronary artery
bifurcation with coronary artery disease.

Material and Methods

Patient datasets

Fifty consecutive patients presenting with typical chest pain indicative of CAD were
screened for study participants over a period of 12 months. Out of these patients, 20
patients were excluded either due to normal coronary artery identified on coronary CT
angiography or because of renal insufficiency, hypersensitivity to iodinated contrast
materials and known severe coronary artery disease. Eight patients with right coronary
artery disease detected on coronary CT angiography were further excluded from the
analysis as this study only focused on the left coronary artery disease. The remaining 22
patients (15 males, 7 females) were included and subjected to invasive coronary
angiography for further analysis of CAD extent. Patient’s characteristics are shown in
Table 1. Fig. 1 shows an example patient, with a stenosis at the left main stem branch. All
patients underwent coronary CT angiography, which was performed on a 64-slice scanner
(GE Medical Systems, Lightspeed VCT, 64x0.625 mm) with the following protocols:
beam collimation 0.625 mm, pitch 0.2-0.26, reconstruction interval of 0.4 mm, with tube
voltage of 120 kVp and tube current ranging from 300 to 650 mAs. Axial images were
reconstructed with a slice thickness of 0.625 mm in 0.4 mm increments, resulting in
isotropic volume data with a voxel size of 0.4 x 0.4 x 0.4 mm³. CT volume data was used
to reconstruct the actual 3D luminal models. Volume data post-processing was performed on a workstation equipped with Analyze 7.0 (Analyze Direct, Inc., Lexana, KS, USA).

Image segmentation was used with a semi-automatic method with CT number thresholding, and scan-related artifacts and soft tissues were manually removed in 2D axial slices [14,15]. The segmented 3D luminal models were created with an emphasis on the left main coronary bifurcation, which is composed of left main stem (LMS), left anterior descending (LAD), left circumflex (LCx), and its side branches. The 3D luminal models of twenty two patients were saved in ‘STL format’ for the generation of computational geometries. Blender version 2.48 (Blender Institute, Amsterdam, Netherlands) was used to reconstruct the 3D computational models. The twenty two geometries of arteries around the LMS, LAD and LCx were obtained from the patient datasets.

The stenosis boundaries were kept in original form from all anatomical structures that were shown on the CT images at left main bifurcation and its side-branches. The luminal surface geometries, consisting of stenosis boundaries, were converted into solid geometries and saved in ‘STL format’ for the meshing methodology.

Types of stenosis in the left coronary artery bifurcation

The coronary CT angiography images were used to classify the type of bifurcation stenosis at the left coronary artery in all patients [3]. These twenty two patients were classified according to the types of bifurcation stenosis: A) stenosis involving the ostium of the LCx and LAD branches; B) stenosis involving the ostium of the LCx branch; C) stenosis involving the LMS branch; D) stenosis involving the ostium of the LAD branch.
The percentage of stenosis lumen was calculated based on measurements on CT images, as shown in Table 1. The diagram of stenosis classification of different types based on the patient datasets was shown in Fig. 2.

**Flow computation and solution**

All realistic left coronary geometries were reconstructed with inclusion of the stenosis boundaries. The sample of four patients, with the different types of bifurcation stenoses in the left coronary artery is shown in Fig. 3. Meshes were created for these geometries, with resolutions ranging from $9 \times 10^5$ to $9.8 \times 10^5$ cells. Mesh independence tests were performed for all coronary geometries. ANSYS ICEM CFD version 12 (ANSYS, Inc.) was used for the meshing process, with details having been described in previous studies [2,16,17]. Transient flow replicating systolic and diastolic phase at the left coronary artery was applied as an inflow boundary condition at LMS [18]. The outflow boundary condition was applied with the flow ratio through the side-branches at the LAD and LCx [19]. Murray's law was used to define the flow relationship between inflow and outflow planes [20]. Rheological parameters were applied, with a blood density of 1060 kg/m$^3$, blood viscosity of 0.0035 Pa s [21]. Blood flow was assumed to be laminar. The blood was assumed to be a Newtonian and incompressible fluid [21]. Blood vessels were assumed to be rigid, and a no-slip condition was applied at the walls [22]. The Navier-Stokes equations were solved using the ANSYS CFX version 12 (ANSYS, Inc.) on a Microsoft Windows 7 32-bit machine, 6 GB of RAM with a Xeon W3505 2.53 GHz CPU. Each timestep was converged to a residual target of less than $1 \times 10^{-4}$. ANSYS CFD-Post version 12 (ANSYS, Inc.) was used to calculate and visualize flow velocity and wall shear stress (WSS).
The WSS is a commonly used factor in hemodynamic analysis; endothelial cells have
been shown to align themselves with the flow direction that corresponds to the local
WSS. The coordinates of the wall surface elucidate the interaction of instantaneous WSS
vectors and endothelial cells [23]. The WSS is defined as:

\[
WSS = \frac{1}{T} \int_0^T \mu \frac{\partial v_t}{\partial n} \, dt
\]  

(1)

where \( \mu \) is blood viscosity, \( v_t \) is velocity vector near wall perpendicular to surface and
\( n \) is distance to the wall surface, \( T \) is pulsatile period, \( dt \) is the time derivative of the
local shear stress. In addition, the time-averaged WSS (TAWSS) [23] for one cardiac
cycle was calculated to include the range of WSS. The range of WSS was calculated
during one cardiac cycle, and the minimum WSS values are approximately 0 Pa and
maximum WSS values are around 3.5 Pa at the left coronary artery bifurcation.

Results

The classification types of realistic bifurcation stenosis among twenty two patients are
represented in Table 1. Fig. 3 shows patients with these four types of stenosis. Ten
patients had type D stenosis (LAD branch) and seven patients had stenosis type A (LAD
and LCx branches). Three patients had stenosis type B (LCx branch) and remaining two
patients had stenosis type C (LMS branch).

Hemodynamic patterns in the left coronary artery bifurcation

Flow patterns were calculated and compared in all types of bifurcation stenosis, as shown
in Fig. 4. The velocity contour levels ranged from 0 mm s\(^{-1}\) to 30.50 mm s\(^{-1}\) with 2.18
mm s\(^{-1}\) between levels. Fig. 4A shows the bifurcation stenosis at the LCx and LAD, and
this case revealed a type A stenosis. The high velocity surrounding the bifurcated location was found at the LCx and LAD, which ranged from 6.54 mm s\(^{-1}\) to 10.89 mm s\(^{-1}\) and 13.07 mm s\(^{-1}\) to 17.43 mm s\(^{-1}\), respectively. The type B stenosis was shown in Fig. 4B, and a high velocity near the bifurcation was reached, from 8.71 mm s\(^{-1}\) to 13.07 mm s\(^{-1}\) at LCx branch. Fig. 4C shows the stenosis involving the LMS branch (type C) and a high velocity was reached, ranging from 6.54 mm s\(^{-1}\) to 8.71 mm s\(^{-1}\), which is close to the bifurcation region. Type D stenosis represented patients who had stenosis at the LAD, and a high velocity close to the bifurcation ranging 17.43 mm s\(^{-1}\) to 19.61 mm s\(^{-1}\). In this analysis the velocity change was found to be high at the stenosis located near the bifurcation areas. The flow variation during diastolic phase was similar to the systolic phase, as the stenosis resulted in high velocity surrounding the bifurcation locations.

Wall shear stress in the left coronary artery bifurcation

Wall shear stress was calculated and compared in all patients with the various bifurcation stenoses, as shown in Table 2 and Fig. 5. TAWSS for all comparisons in one cardiac cycle was calculated in addition to the range of WSS, as shown in Table 2. WSS distributions were mainly plotted to present the effects of lumen stenosis at the left coronary artery bifurcations. Calculated WSS values during cardiac cycle ranged from 0 Pa to 3.50 Pa. Fig. 5A shows the impact of stenosis at the LCx and LAD close to the bifurcation, representing patient who had type A stenosis. WSS values were found, to range from 1.75 Pa to 2.0 Pa and 2.25 Pa to 2.5 Pa, at LCx and LAD branches respectively. Fig. 5B demonstrates that the WSS values at LCx ranging from 3.25 Pa to 3.5 Pa, which represented the type B stenosis. In addition, the stenosis at LMS had minor effects on WSS changes, which values ranged from 0.75 Pa to 1.0 Pa near the bifurcation.
Fig. 5C. Fig. 5D shows stenosis located at LAD branch with WSS were found to range from 3.25 Pa to 3.5 Pa.

Fig. 5 shows the patient with a long LMS branch and a 30% stenosis displayed minor WSS change at the stenosis locations (arrows in Fig. 5C), while other patients showed WSS to be high at locations close to the bifurcations (Fig. 5A, B and D). In all patients at the locations of stenosis, low WSS was defined as < 1 Pa, intermediate WSS as >= 1 Pa to < 2.5 Pa, and high WSS as >= 2.5 Pa. High WSS was found in coronary branches where a >70% stenosis was present, and in the group of patients who presented with high WSS at stenosis regions (Fig. 5B and D, arrows). The range of WSS in each type of bifurcation stenosis that was detected in all patients with CAD, can be grouped into 4 categories based on our study population. TAWSS changes were similar to WSS changes in all types of stenosis but the averaged WSS values for all time steps of computation varied about 0.25 Pa of WSS values which reached at time of 0.2 s in systolic phase during one cardiac cycle. The WSS demonstrated changes during both systolic and diastolic phases, and the WSS levels were dependent on the stenosis types and degree of lumen stenosis, as shown in Fig. 2.

Table 3 represents the range of WSS in each type of bifurcation stenosis that was detected in patients CAD, which can be grouped into 4 categories. Stenosis type A showed a large WSS change of 0.715 Pa, and patient who had 30% stenosis represented WSS change of 0.50 Pa. Stenosis type B and D showed small WSS change of 0.25 Pa, and most of the patients in these two types had stenosis >= 50%. Stenosis type C demonstrated the WSS change of 0.50 Pa. Therefore, the WSS variation in stenosis type A demonstrated the highest WSS values changes when compared to other types of stenosis.
Discussion

This study investigated the flow change and WSS distribution in the left coronary, based on different types of stenosis from a group of patients presenting with coronary artery disease. The datasets used consisted of reconstructions of the realistic left coronary geometries of 22 patients. Our results showed the various hemodynamic changes due to different types of stenosis, mainly due to the involvement of different left coronary branches. Thus, our study has potential value for improving the understanding of the impact of various types of bifurcation stenosis, and accordingly, the coronary artery disease.

Coronary artery disease generally forms near the bifurcation, due to the blood vessel’s inherent angulation and tortuosity, leading to low WSS [2,3,8]. Medical imaging techniques such as CT angiography provides excellent anatomical details of the coronary lumen changes, however, they are unable to provide hemodynamic factors such as WSS distribution and flow variation. Recent studies have used computational fluid analysis to overcome the limitations of imaging modalities by characterizing hemodynamic changes in the situation of coronary disease [9-13]. Many studies reported in the literature paid attention to the degree of stenosis and the effects of stenosis originating in the left coronary artery bifurcation and side-branches and subsequent hemodynamic changes [9-13]. There is very little research being conducted, correlating hemodynamic change with the various types of bifurcation stenosis in the left coronary artery. This study was conducted to fill in the gap in the literature.

This study focuses on two important factors: velocity and WSS, and the characterization of the flow patterns and WSS variations at stenotic locations in left main coronary
bifurcation. The velocity was found to increase at stenotic locations in all types of
bifurcation stenoses (as indicated with arrows in Fig. 4). Factors that influence the
velocity increase, include vessel diameter, bifurcation angle, vessel tortuosity [2, 5, 6, 9-
11]. In the coronary arteries, flow is highly pulsatile, with reversing flow in systole, and
high forward flow in diastole. The left coronary artery consists of two main branches,
LAD and LCx, which feature curvature in multiple phases. The likelihood of low WSS is
high, depending on the individual geometry [24]. It has been reported in a previous study
involving 17 casts of left coronary bifurcation that there is considerable variability in the
left LAD and LCx geometries among patients, with the proximal segments of the LAD
and LCx being the most predisposed sites to atherosclerotic disease [25]. Zhu et al
characterized the normal geometry in 32 LAD and 35 right coronary arteries, and their
results further confirmed the presence of considerable geometric variability in the
coronary vasculature, particularly in the LAD [26]. Our analysis is consistent with these
reports, showing that the geometric parameter in the left coronary artery induces a
corresponding variability in the mechanical environment of the vessel, which would most
likely to be responsible for individual differences in disease susceptibility and
localization.

WSS affects biological signals to mechanoreceptors in endothelial cells, and it can affect
gene expressions causing changes to the cellular functions of vessel walls [27,28]. In our
analysis, WSS levels (low, intermediate and high) are in line with previous reports [27-
29]. High WSS is also indicated as a contributor to the rupture and thrombosis of
advanced atherosclerotic in human coronary artery [29-31]. Therefore, it could be
assumed that patients having stenosis at LAD branch (Fig. 5B) could lead to the plaque rupture, although this needs to be verified in further analysis.

Several limitations in this study should be addressed. Firstly, the walls of vessels were assumed to be rigid, a reasonable assumption in this case, supported by previous studies [22]. Secondly, the blood was assumed to be Newtonian, and this assumption is also supported by previous studies [7,21]. Thirdly, the study population was restricted to a small number of patients that can only be classified into the four types of bifurcation stenosis at the left coronary artery. In this study, we aim to characterise the stenosis type only based on the location of stenosis in the left coronary artery and to report the effects of the stenosis type with quantitative analysis of main hemodynamic factors such as velocity and wall shear stress. Therefore, future studies will use more patient’s data, representing various types of actual stenosis, including all possible disease conditions in the left main coronary artery.

In conclusion, this study investigates the effects of stenosis on WSS and flow variation at bifurcated regions, and the patients’ datasets were classified into the four types of bifurcation stenosis. WSS and flow velocity was found to change at different stenosis locations. WSS at >70% stenosis was significantly different from that observed at <30% of stenosis. Stenosis type A demonstrates large WSS changes, while stenosis type B and D show small WSS changes. Our results complement the former studies and have the potential of providing new insights and additional information about the hemodynamic effects of plaque location and coronary stenosis, thus, improving the understanding of the hemodynamic characterization of realistic bifurcation stenosis, although further studies based on a larger cohort are needed to confirm our results.
Conflict of interest statement: All authors declared that they did not have any financial and personal relationships with other people or organisations that could inappropriately influence their work.
References


**Figure legends**

Fig. 1. 2D medical imaging shows significant stenosis at left main stem due to calcified plaque, (arrow in A); corresponding virtual endoscopy confirms the lumen stenosis by demonstrating intravascular appearance (arrows in B).

Fig. 2. The diagram shows classification system of bifurcation stenosis in the left coronary artery with stenosis involving LAD and LCx (A), LCx (B), LMS (C), and LAD (D).

Fig. 3. The selected geometries of realistic left coronary models with bifurcation stenosis based on the classification system in Fig. 2, (A) stenosis type A in patient No. 1, (b) stenosis type B in patient No. 7, (c) stenosis type C in patient No. 16 and (d) stenosis type D in patient No. 10. Arrows reveal the stenosis locations.

Fig. 4. Flow patterns of velocity change surrounding bifurcation were reached at time of 0.2 s in systolic phase during one cardiac cycle in patients who had (A) stenosis type A, (B) stenosis type B, (C) stenosis type C and (D) stenosis type D. Arrows identify the velocity to be high at stenosis positions near the bifurcations.

Fig. 5. WSS distributions of WSS change surrounding bifurcation were reached at time of 0.2 s in systolic phase during one cardiac cycle in patients who had (A) stenosis type A, (B) stenosis type B, (C) stenosis type C and (D) stenosis type D. Arrows identify the WSS to be high at stenosis positions nearby bifurcations.