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A Computational Study of Curvature Effect on the Coronary Diagnostic Parameters in Stenosed Coronary Artery

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Keyword：Coronary artery, Stenosis, non-Newtonian, FFR.

ABSTRACT

The presence of downstream curvature can affect the blood flow in artery leading to complicated hemodynamics. Thus, the current study is focused to explore the effect of downstream curvature of artery wall on the severity of stenosis by assessing the Fractional Flow Reserve, Lesion Flow Coefficient and Pressure Drop Coefficient under various downstream curvature angles in coronary artery. Computational fluid dynamics (CFD) of hyperemic flow in curved arteries was performed with various downstream curvature angles (0^0 30^0 60^0 90^0 and 120^0) subjected to three different blockage (70%, 80% and 90%) area stenosis (AS). It is discovered that flow resistance caused by stenosis increases further due to the downstream curvature of artery. The FFR decreased by 5.4%, 8.6% and 13.1% for 70%, 80%, and 90%AS respectively as the downstream curvature of artery increased from 0^0 to 120^0. The increase in CDP and decrease in LFC was found as the downstream curvature increased from 0^0 to 120^0. The differences in diagnostic parameters FFR, CDP and LFC shows that misinterpretation could be possible while evaluating the functional significance of stenosis, so the downstream curvature must be contemplated while evaluating the importance of stenosis as an additional parameter for FFR.

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INTRODUCTION

Coronary artery disease (CAD) is one of the major heart diseases which leads to millions of deaths across the globe. The key reason of CAD is atherosclerosis, which is a buildup of cholesterol and other material inside the artery wall, consequently causing lumen narrowing, i.e. stenosis. The complexity in the geometry of coronary arteries and the hemodynamics play a vital role in the growth of stenosis. Atherosclerotic plaque advances in the artery's branches, aortic T-junctions, bent segments, and artery bifurcations where complex spiral secondary flow zones, recirculation, and low wall shear are formed [Wang and Li, 2011]. Many CFD studies reported the effect of arterial geometry on the wall shear stress and hemodynamic factors by developing either idealized coronary models [Huang et al., 2009; Chaichana et al., 2011; Soulis et al., 2006; Van Wyk et al., 2013: 2014; Zakaria et al., 2008] or by reconstructing coronary arterial models through image processing which includes CT, MRI, IVUS and Angiography Goubergrits et al., 2008; Gijsen., 2007]. In mathematics, the amount by which a vessel deviates from being linear is measured by the curvature1. Vessels with a lesser radius of curvature (or larger curvature), bend more sharply. Therefore, the effect of downstream curvature is significant in a stenosed curved arteries. The assessment of physiological significance of intermediate stenosis is challenging for cardiologists [Tobis et al., 2007]. Currently, in the medical field, Fractional flow reserve (FFR) is a clinically established diagnostic criteria for evaluating the functional significance of stenosis [Pijls., 1995; 2012]. A number of clinical studies showed that FFR more than 0.8 are not linked with exercise-induced ischemia in a single vessel coronary artery disease. In cases where FFR falls below 0.75, the patient is advised to undergo an angioplasty or coronary artery bypass graft (CABG) [Kern et al., 2010; Hau., 2014]. An intracoronary pressure wire ,0.014 inch in diameter, is used to carry out the functional diagnostic parameter FFR for recording distal pressure at hyperemic condition, papaverine or adenosine. [Pijls., 1995]. Apart from FFR, CDP and LFC are diagnostic parameters which are procured from the fundamental fluid dynamics principles, which help in identifying the graveness of stenosis. Many researchers studied the variation of FFR due to the introduction of guide wire [Sinha Roy., 2006], collateral flow at downstream [Peelukhana et al., 2009] and other factors including aortic and coronary outflow pressure [Siebes et al., 2002], microvascular resistance, and compliance of arterial wall. Characteristics of any plaque notably affect value of FFR [Konala et al., 2011]. The length of stenosis and geometrical shapes significantly affect the FFR. Several studies by computational simulation reported on the hemodynamic parameter changes in the curved stenotic arteries [Yao et al., 2000; Chaniotis et al., 2010; Santamarina et al., 1998; Liu 2009]. A limited research focused on the implication of downstream curvature on the coronary diagnostic parameters. Therefore, the current investigation studies the implication of downstream curvature on the coronary diagnostic parameters in various degree of percentage area stenosis.

METHODOLOGY

The current research is based on the 3D computational models of 0^0, 30^0, 60^0, 90^0 and 120^0 downstream curvature of a stenosed coronary artery. L1 and L3 represent the length prior to the stenosis and immediate after the downstream curvature which is 30mm and 40mm respectively. The downstream curvature length L2 for all the models under investigation is kept at a constant value of 10mm. Fig. 1. shows the geometric representation of an ideal stenosed curved artery model. The various size of stenosis was introduced prior to the downstream curvature in the coronary artery models. The percentage area stenosis was evaluated using equation (1). Table 1 shows the length and dimension of stenosis considered in the current study [Konala et al., 2011; Govindaraju., 2014]. All computer aided designed artery models were imported into the meshing software ICEM CFD 14.5 for meshing. The models have meshed with hexahedral elements consisting of 339625 numbers of elements. The mesh independent study was executed to ensure that the selected number of elements is a right choice, the details of mesh independent and grid structure generated for the 30 degrees curved artery for 70%AS is as shown in table 2, fig. 2a and figure 2b respectively. The area stenosis can be calculated as:

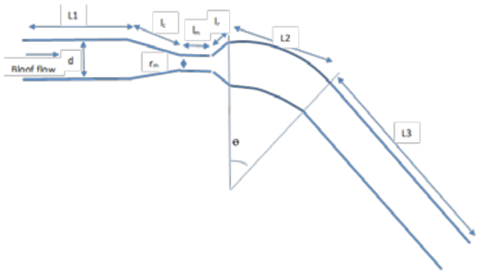


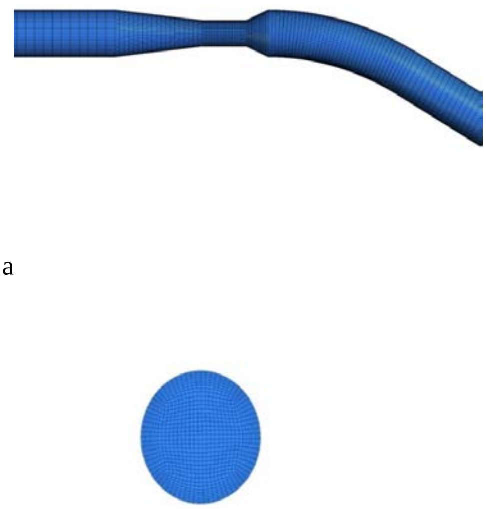
Fig. 1. Downstream curved stenosed artery.

Table 1. Dimensions of different degree of stenosis in the models (All the dimensions are in millimeter) [Govindaraju et al., 2014; Konala et al., 2011]

Area stenosis (AS)	d	r_m	l_c	l_m	l_r
70 %	3	0.82	6	3	1.5
80 %	3	0.67	6	1.5	1.5
90 %	3	0.47	6	0.75	1.5

Table 2. Mesh independent study for Straight model of 70% AS

Straight model of 70% AS	No of elements	Time in (Hr:min:s)
Mesh 1	245385	2:38:54
Mesh 2	339625	2:46:26
Mesh 3	460275	3:01:36



a

b

Fig. 2. Grid structure for the curved stenosis artery of 30 degree is shown in the figure (a) longitudinal section (b) cross section

Computational Modelling

The governing equations will be the Navier-Stokes equations, with blood being incompressible and a non-Newtonian fluid.

$$\rho\left(\frac{\partial v}{\partial t}+v.\nabla v\right)=\nabla.\tau-\nabla P \qquad (2)$$

Continuity equation for the above condition is:

$$\nabla.v=0 \qquad (3)$$

Here v is the velocity vector in three-dimension, being blood density, t is the time, is the stress tensor and P is the pressure.

The equation governing the Non-Newtonian and Bird-Carreau model is given by

$$\mu=\mu_\infty+(\mu_0-\mu_\infty)[1+(\lambda\gamma)^2]^{(n-1)/2} \qquad (4)$$

Where λ represents Time constant = 3.313s, μ_0 being low shear viscosity = 0.56 P, n (Power law index) = 0.3568, μ_∞ (High shear viscosity) = 0.0345 P, γ shear rate and blood density (ρ) is assumed to be 1050kg/m^3 [Kamangar et al., 2014; Kamangar et al., 2017]. The simulations were carried out using a finite volume software called CFX17.2 (ANSYS Inc). [Kamangar et al., 2017; Kamangar et al., 2017].

Boundary conditions

A transient parabolic velocity at the inlet (u(t)) (Fig.3) [Konala et al., 2011; cho et al., 1983; Govindaraju et al., 2016], static pressure of 80mmHg at outlet and no slip condition at the artery wall were applied as boundary conditions in order to carry out the 3D numerical simulation, in effort to mimic the real physiological conditions [Kamangar et al., 2017]. The inlet and outlet boundary conditions were identical for computation of all models. The mean hyperemic flow rate (Q) 175ml/min, 165ml/min and 115 ml/min was used to acquire the velocity profile for 70 percent, 80 percent and 90 percent AS respectively [Konala et al., 2011, Roy et al., 2015]. The shear stress transport (SST) turbulence model, belonging to k-ω model family, is used to carry out the present study. The mean throat Reynolds numbers for 70 percent, 80 percent and 90 percent AS were 647, 747 and 742 respectively. The persistence of the instabilities in shear layer due to the disruptions in cardiac pulse and non-uniformity in the plaque anatomy under hyperemic flow conditions [Banerjee et al., 2013; Mallinger et al., 2002] could lead to the turbulent flow. Initially, the flow analysis was carried out for the steady state conditions, and the outcomes of the steady state condition were made as an initial guess for further transient conditions. Figure 3 shows the normalized applied inlet velocity ($\bar{u}/\bar{u}_{p-t}$). The ratio of mean to peak velocity ($\bar{u}/\bar{u}_{p-t}$) is 0.537.

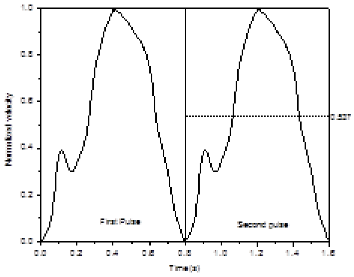


Fig. 3. (a) Inlet velocity

Diagnostic Parameter

Fractional flow reserve

The ratio of distal coronary pressure to aortic pressure, at hyperemia, is known as FFR [Pijls et al., 1995; Pijls et al., 2012].

$$FFR=\frac{\tilde{p}_d-\tilde{p}_v}{\tilde{p}_a-\tilde{p}_v} \qquad (5)$$

where $\tilde{p}_d$ is time averaged distal stenotic pressure (mmHg), $\tilde{p}_v$ is venous pressure taken as 0 mmHg. $\tilde{p}_a$ is time averaged aortic pressure (mmHg),

Pressure drop coefficient:

CDP is a derived non-dimensional functional parameter, at hyperemia, based on principles of fluid dynamics considering time-averaged pressure drop ($\Delta\tilde{p}$) and proximal velocity at stenosis (Konala et al., 2011; Banerjee et al., 2007).

$$\mathrm{CDP}=\frac{\Delta\tilde{p}}{0.5\rho U_a^2} \qquad (6)$$

Where $\Delta\tilde{p}=(\tilde{p}_a-\tilde{p}_d)$ (N/m2) and Ua is the proximal velocity in ms^{-1}. CDP accounts for both, viscous loss and loss caused by change in momentum in the flow across the stenosis.

Lesion flow coefficient:

Lesion flow coefficient (LFC), a normalized and dimensionless functional diagnostic parameter, was formulated by Banerjee et. al., 2007, by taking into account the geometric parameters and the functional endpoints. It is the ratio of %AS and the square root of CDP calculated at stenosis site and it ranges from zero to one.

$$\mathrm{LFC}=\frac{percentage\ AS}{\sqrt{\Delta\tilde{p}/0.5\rho U_{(a-h)}^2}} \qquad (7)$$

Where $U_{(a-h)}$ represents stenosis site velocity in ms^{-1}

Statistical analysis of coronary diagnostic parameters

The statistical analysis was carried out for computed data of, CDP, FFR and LFC in all configurations. A One-way repeated measure ANOVA with post hoc Tukey's test was utilized for comparison of computed data to ascertain the differences in the curvature. The purpose of this analysis was to check the differences in above said values with respect to curvature angle. This helps to evaluate the differences between the means of different groups of data that further examines its statistically significant though a parameter known as p-value to assess the null hypothesis. Generally, a significance level of 0.05 is adopted (as in present study) that works very well. A 0.05 significance level means that 5% risk of concluding that a difference exists when there is no actual difference.

RESULTS AND DISCUSSION

Diagnostic parameter comparison

Results show that, for provided percent area stenosis, there were notable differences in LFC, $\Delta\tilde{p}$, CDP and FFR between curved artery and straight artery models as tested above mentioned ANOVA ($p< 0.05$). The post hoc test highlighted that LFC, $\Delta\tilde{p}$, CDP and FFR between 30 degree and 60 degree ($p>0.05$), 60 degree and 90 degree ($p>0.05$) and 90 degree and 120 degree ($p > 0.05$) were not significant. However, these parameters in the remaining pairwise combination of curvature were statistically significant ($p<0.05$).

Change in pressure drop due to downstream curvature

Figure 4 presents the time average pressure drop for various downstream curvature angles. For a particular percentage area stenosis, the time average pressure drops increase with increase in downstream angle of curvature. The significant increase in pressure drop was found as the downstream curvature increases for a given percentage area stenosis. An increment in time average pressure drop from 6.34mmHg to 9.71 mmHg, 12.13 mmHg to 17.8 mmHg, and 25.99 mmHg to 34.62 mmHg was found as the curvature increased from 00 to 1200 for 70%, 80%, and 90%AS models. These findings imply that downstream curvature raises the resistance to the flow in addition to the resistance caused by the presence of area stenosis. Therefore, the highest-pressure drop was observed for a minimal cross section area (90%AS) and the downstream curvature aids to the extra drop in pressure in the curved coronary artery.

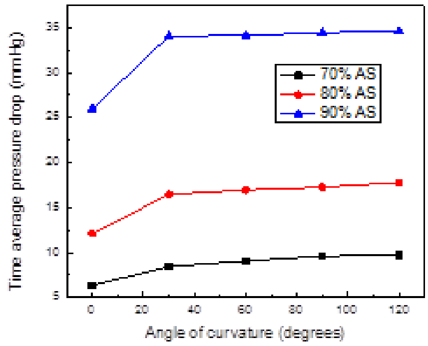


Fig. 4. Figure showing time averaged pressure drop variation across the stenosis for 70 percent, 80 percent and 90 percent AS with various angle of curvature

Changes in coronary diagnostic parameters due downstream curvature

Changes in FFR due to downstream curvature

Figure 5 highlights significant decreases in FFR as the percentage areas stenosis increases. It is also found that as the downstream curvature increases the FFR decreases for a given percentage area stenosis in stenosed curve artery. As the downstream curvature angle changed from 0 degree to 120 degree, the FFR decreased from 0.91 to 0.86 (5 percent), 0.81 to 0.74 (8 percent) and 0.61 to 0.53 (13 percent) in 70 percent, 80 percent and 90 percent AS coronary models respectively. These results show that the appearance of downstream curvature in stenosed artery contributes to the additional decrease in FFR. The highest decrease in FFR was observed for severe stenosis (90%AS) as compared to intermediate stenosis (70%AS, and 80%AS). A line being the best fit curve (R2 = 0.97) was fitted in the data set of the computed values of FFR values as shown in Figure 6. In Figure 6, a horizontal line was drawn at the cut-off value of FFR = 0.75 so as to determine a range of AS resulting from possible misdiagnosis. This horizontal line intercepted the FFR-AS lines at 77.43% and 81.63% in straight and 120-degree curve artery.

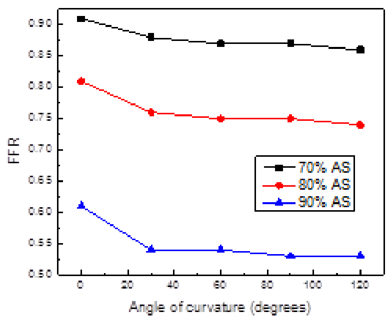


Fig. 5. FFR variation with the angle of curvature in 70%, 80% and 90% AS models.

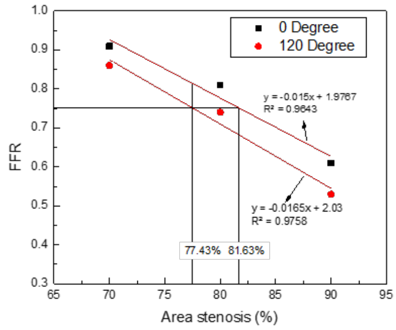


Fig. 6. FFR variation with curvature angle. Corresponding to FFR=0.75, a non-linear trend line was fitted to FFR data for 0 degree and 120-degree models

Changes in CDP and LFC due to downstream curvature

The variation of CDP and LFC for different angles of downstream curvature is depicted in figure 7 and figure 8 respectively. The CDP and LFC were calculated by using pressure difference, flow and stenosis geometry in all the severity models. For a provided percentage area stenosis, the CDP increases from 9.43 to 14.46, 20.35 to 29.87 and 89.86 to 119.71 in 70% 80% and 90%AS, respectively. Whereas the LFC decreases from 0.76 to 0.61, 0.88 to 0.73 and 0.96 to 0.83 in 70%, 80% and 90%AS respectively. These results show that with increment in the downstream curvature angle from 00 to 1200, decrement in LFC was observed.

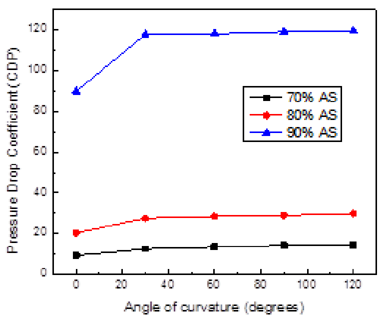


Fig. 7. Figure shows CDP variation with curvature angle in 70%, 80% and 90% AS models

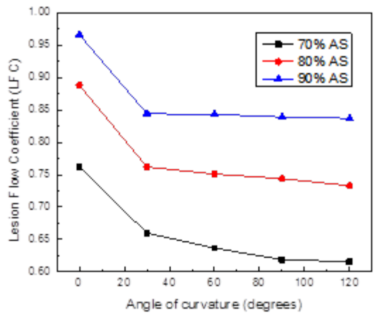


Fig. 8. Figure shows LFC variation with angle of curvature in 70%, 80% and 90% AS models

The present investigation studies numerically the effect and outcomes of the downstream curvature angle of the stenosed curved artery on LFC, CDP and FFR for a provided percentage AS. These findings provide extra information about the hemodynamic effect of downstream curvature in stenosis curved artery; hence it enhances the interpretation of in vitro assessment of stenosis severity from the FFR perspective.

As the percentage area stenosis increases the $\Delta\tilde{p}$ increases across the stenosis and this owes to the difference in momentum caused by the increment in flow velocity across the stenosis configuration. The significant difference by statistical analysis was observed in pressure drop for a fixed percentage area stenosis and pressure derived FFR between straight and downstream curved arteries. Figure 9 clearly shows the axial flow velocity skewed towards the outer wall because of centrifugal pressure gradient associated with the secondary flow and leads to additional pressure drop along with the area contraction before the curvature. This discovery is congruous with the results of Yao et al., 2000 It is observed that the drop-in pressure significantly increases as the downstream curvature angle of the artery increases.

The current results show that the value of FFR calculated across the stenosis is significantly higher in 0-degree downstream curvature as compared with the 120-degree downstream curvature stenotic model for a given percentage area stenosis. FFR deduced from drop in pressure across the stenosis decreases with the increase in percentage area stenosis. Figure 10 shows a comparison of FFR for straight stenosed artery models obtained in the present study with the numerical results presented previously by Konala et. al., 2011, for 70 percent, 80 percent and 90 percent AS with rigid wall and rigid plaque models.

The FFR value highlights the functional severity of stenosis. It is seen that FFR values lesser than 0.8 is functionally significant. Clinicians propose an angioplasty or coronary artery bypass graft (CABG) if FFR drops less than 0.75. For FFR values more than 0.8, surgical procedures may be avoided and the patient can be put under medications and medical therapies. Thus, FFR can provide an approach to the clinician's proceeding in further medical treatment. The FFR gray zone comprises a meagre 5 percent difference (0.75 to 0.80), which lies under intermediate stenosis severity. The variation in downstream curvature of the artery strongly affect the drop-in pressure across the stenosis and hence the FFR, for a provided %AS, as confirmed by the current study. For AS <77.43%, the FFR values for both the models (0 and 120 degrees) were significantly above the cut-off value of 0.75 and for AS < 81.63%, the FFR value for 120-degree curved model was observed below the cut-off value whereas the other models (0 degree) show above the cut-off value of 0.75 which could lead to the misdiagnosis of stenosis severity. A region of uncertainty was found, in assessment of the anatomical significance of stenosis severity, between 77.43% and 81.63% AS by plotting a linear approximate correlation between FFR and per cent AS. The numerical analysis is performed in order to present evidence of the impact of curvature of the artery wall on the anatomical assessment of stenosis severity that needs to be tested in human arteries.

Similarly, the computed values of CDP and LFC by varying the downstream curvature in 70% 80% and 90% AS are not directly used as clinical diagnostic parameters, instead, these parameters provide additional information to FFR to obtain the outright scenario of the functional significance of the stenosis severity. These parameters require the measurements of flow/pressure wire whereas FFR needs only the pressure to estimate the severity of stenosis. There for cut-off values for these parameters should be defined in order to evaluate the diseased artery clinically.

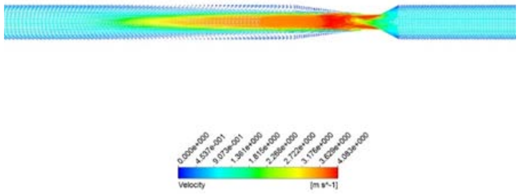
The current study proves that the complex morphological geometry of the stenosed artery plays a significant role along with the anatomical parameter such as area stenosis for estimating the functional significance of stenosis severity through FFR. The detection of ischemic stenosis and visualization of coronary artery disease by a non-invasive technique such as CCTA demonstrates with high accuracy. Notably, the difference in the percentage of FFR between 0 straight model and 120-degree curved model is 8.6% in 80%AS models. This significant difference confirms that the misdiagnosis could be possible if the downstream curvature of a stenosed artery neglected while assessing the stenosis severity of intermediate stenosis.

There are some shortcomings of the study which needs to be addressed in future

1) The realistic coronary models should be used in order to deal with the shortcomings to analyze the influence of curvature of the artery wall on anatomical estimation of stenosis severity

2) The important factor which could affect the coronary diagnostic parameters like, arterial wall compliances, various bends, and dynamic curvature variations due to heartbeat, wall roughness, lesion eccentricity, tandem lesion and diffused disease were not included in the study.

3) The coronary models considered in the current study assumes to have rigid artery wall rather than elastic. Therefore, the simulation does not exactly mimic the real physiological conditions.



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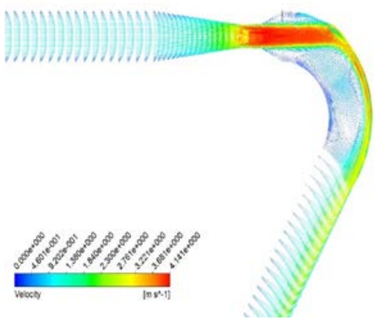

b

Fig. 9. Secondary flow development in a) straight and b) curved artery model for 80%AS

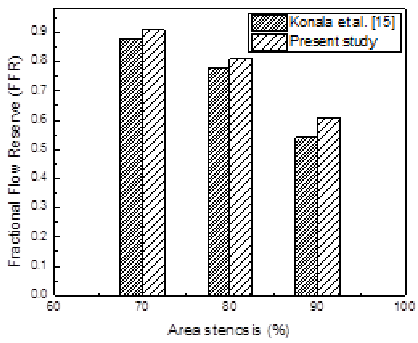

Fig. 10. Figure showing FFR values, obtained numerically, compared with B.C Konala et al., 2011, in straight stenosed coronary artery models for the 70 percent, 80 percent and 90 percent AS

CONCLUSIONS

The effect of downstream curvature angle on the coronary diagnostic parameters in 70 percent, 80 percent and 90 percent Area Stenosis coronary artery model under hyperemic conditions was investigated by using CFD. The results show that for a given percentage area stenosis, a significant variation in the diagnostic parameters LFC, FFR and CDP was found between the straight and curved artery models. The computed diagnostic parameter FFR decreases by 5.4%, 8.6% and 13.1% for the 70%, 80%, and 90%AS respectively as the downstream curvature of artery increased from 00 to 1200. As the angle of downstream curvature increases from 00 to 1200 the value of CDP increases, whereas the value of LFC decreases. The significant differences validate that the non-invasive evaluation of stenosis leads to misdiagnosis of the severity of stenosis. It is suggested that apart from the stenosis size, shape and its compliance the downstream curvature of the arterial wall affect the visual assessment of stenosis severity, particular for the case of intermediate stenosis.

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