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CFD Simulation of Density Variation Caused by Anti-platelet Drug in Arteries Affected by Stenosis

H. Girija Bai*

Sathyabama University, Chennai-600 119, Tamil Nadu, India; girijanameprakash@gmail.com

Abstract

In this paper, a mathematical model has been developed for studying unsteady blood flow through the stenosed vessel under different density variation due to antiplatelet drug. Blood flowing through the artery is considered to be Newtonian. By considering 25% and 90% dilations in arteries, expressions for the velocity profile, wall shear stress, streamline pattern and pressure gradient have been derived numerically under finite volume method. The above said quantities are computed for a specific set of values for different parameters involved in the model analysis. This serves as an illustration of the validity of the mathematical model developed here. The results estimated on the basis of the computation are presented graphically. The obtained results for different parameters involved in the problem show that the flow is appreciably influenced by density variation at different time seconds.

Keywords: Antiplatelet Drug, Density Variation, Finite Volume Method, Graphically, Mathematical Model, Newtonian, Parameters, Stenosed Vessel, Streamline Pattern, Velocity Profile; Wall Shear Stress

1. Introduction

In developed countries the majority of deaths are caused by cardiovascular diseases, most of which are connected with some form of irregular blood flow in arteries. The arteries are living organs that can adjust to and change with the varying hemodynamic conditions. Heart disease (Heart and blood vessel disease) includes numerous problems, many of which relate to a process called atherosclerosis. Atherosclerosis is a condition that develops when a substance called plaque builds up in the walls of the arteries. This buildup narrows the arteries, making it harder for blood to flow through. The obstruction may damage the internal cells of the wall and may lead to further growth of stenosis. This vascular disease is of frequent occurrence, particularly in mammalian arteries. If this disease takes a severe form, it may lead to fatality. Although the exact mechanism for the development of this vascular disease is somewhat unclear, various investigators emphasized that the formation of the intravascular plaques and the impingement of ligaments and spure on the blood vessel wall are some of the major factors for the initiation and development of this vascular disease. If a blood clot forms, it can stop the blood flow. This can cause a heart attack or stroke. If this clot cuts off the blood flow completely, the part of the heart muscle supplied by that artery begins to die. Treatment of atherosclerosis of the carotid artery is dependent on the severity and degree of the disease. Mainly two major types of stroke may occur in humans are Ischemic stroke and hemorrhagic stroke. An ischemic stroke (the most common type) happens when a blood vessel that feeds the brain gets blocked, usually from a blood clot. When the blood supply to a part of the brain is shut off, brain cells will die. The result will be the inability to carry out some of the previous functions as before like walking or talking. A hemorrhagic stroke occurs when a blood vessel within the brain bursts. The most likely cause is uncontrolled hypertension. Since the arterial tube is constricted, the recirculation of flow occurs, this leads to abnormal flow of blood and leads to stroke. To overcome that abnormality, the heart pumps blood very fast and the flow gets aggravated that leads to HBP.

*Author for correspondence

Some effects of stroke are permanent if too many brain cells die after a stroke due to lack of blood and oxygen to the brain. These cells are never replaced. Some brain cells don't die — they're only temporarily out of order. Injured cells can repair themselves. Over time, as the repair takes place, somebody functioning improves. Also, other brain cells may take control of those areas that were injured. In this way, the strength may improve, speech may get better and memory may improve. To prevent or to avoid further occurrence of stroke medication is vital. If a blood clot forms inside an artery, it blocks the flow of blood to the tissue that the artery supplies, which can damage the tissue. So the main aim is to remove or to prevent the blood to clot.

Medications used to manage atherosclerotic disease include:

- Antiplatelet ('blood thinner') agents (eg, aspirin, ticlopidine, clopidogrel)
- Anticoagulants (eg, warfarin)

Antiplatelet agents are medications that block the formation of blood clots by preventing the clumping of platelets. Antiplatelet therapy is used for both the management of acute ischemic stroke and for the prevention of stroke. Antiplatelet therapy reduces the incidence of stroke in patients at high risk for atherosclerosis and in those with known symptomatic cerebro vascular disease. There are three types of antiplatelet agents:

1. Aspirin,
2. Tthienopyridines, and
3. Glycoprotein IIb/IIIa inhibitors.

These agents differ in the way they work, their influence, how rapidly they work, and their cost. Aspirin has an important inhibitory effect on platelets in the blood. Aspirin belongs to a class of medications called Non Steroidal Anti-Inflammatory Drugs (NSAIDs). Aspirin is known chemically as acetyl salicylic acid and often abbreviated as ASA. Aspirin is widely used either alone or in combination with other antiplatelet agents to prevent blood clots from forming in arteries. Aspirin prevents blood from clotting by blocking the production by platelets of thrombosane A-2, the chemical that causes platelets to clump. Aspirin accomplishes this by inhibiting the enzyme Cyclo-oxygenase-1 (COX-1) that produces thromboxane A-2. While other NSAIDs also inhibit the COX-1 enzyme, aspirin is the preferred NSAID for use as an antiplatelet agent because its inhibition of the COX-1 enzyme lasts much longer than the other NSAIDs (aspirin's antiplatelet effect lasts days while the other NSAIDs' antiplatelet effects last only hours).

Like aspirin Thienopyridines, the onset of action of clopidogrel (Plavix) is dose related. The maximal antiplatelet effect occurs several days after initiation of clopidogrel (75 mg/daily), but can occur within hours after larger doses of 300 or 600 mg. Therefore, larger doses of clopidogrel are used initially when immediate antiplatelet actions are needed (such as after placement of intracoronary stents) while the lower doses are used as maintenance. The glycoprotein IIb/IIIa inhibitors have a rapid onset of action. Their maximal antiplatelet effect occurs within minutes after an intravenous infusion, and are used mainly in patients with unstable angina or acute heart attack (myocardial infarction). Stopping antiplatelet therapy in high-risk patients may itself increase the risk of stroke.

Heart attack prevention is of two types, primary and secondary. Preventing the first heart attack is called primary prevention. Preventing further heart attacks among patients who already have had a heart attack is called secondary prevention. Within six years after the first heart attack, 16% of men and 35% of women will have a second heart attack. Long-term, daily aspirin (75–325 mg/d) has been shown to reduce the risk of second heart attacks and improve survival among both men and women. Additionally, long-term secondary prevention with aspirin also has resulted in fewer ischemic strokes. Therefore, survivors of heart attacks usually take daily low dose (75 mg–160 mg/d) aspirin indefinitely to prevent further heart attacks as well as strokes.

Aspirin is not the only treatment for heart attacks and unstable angina. Sometimes Percutaneous Transluminal Coronary Artery angioplasty (PTCA), with or without placement of an arterial stent, is necessary to open narrowed or blocked coronary arteries. In rare instances, PTCA may be technically impossible, or not practical, to do, and Coronary Artery Bypass Graft surgery (CABG) becomes necessary to improve the flow of blood to the heart.

Some patients with heart attacks are treated with thrombolytic agents (medications that dissolve clots) to open blocked arteries. It is important to make the distinction that aspirin generally does not open an existing blood clot, but it acts to prevent propagation of the existing clot and the formation of new ones. In all of these instances, there is a risk that blood clots will form again in the arteries, leading to further heart attacks. In all of these cases, aspirin has been shown to be beneficial

in preventing new clots, thus reducing the risk of heart attacks and improving both short and long-term survival.

The homodynamic behavior of the blood flow in arterial stenoses, the impact of different drugs and the antiplatelet reactions bears some important aspects due to engineering interest as well as feasible medical applications. Bart[1], O'Brien[2] analyzed a simple pulsatile flow in an artery with a constriction. Bernardo[3], Jorg[4] and Mittal[5] suggested about the antiplatelet drugs. Huang et al.[6] investigated flow in a tube with an occlusion by using finite difference scheme for steady and unsteady flow. Hua-Bing[7], Mandal[8,9] suggested the effect of different shaped stenoses. Gaivas[10] discussed cerebral aneurysms models and shear stress was discussed by Malek[11] and Mostafa Toloui[12]. John David Folts[13], Philip R. Belcher[14], Rowe[15], William[16] and Yumei Ye[17] suggested the role of drug in vascular disease. Quan Long et. al.[18] made a numerical study to investigate the capacity of the Circle Of Wills (CoW) to provide collateral blood supply for patients with unilateral carotid arterial stenosis. Rathish Kumar and Naidu[19] analyzed a finite element analysis of simple pulsatile flow in a constricted vessel. Lee et al[20], Scott Lovald[21] numerically analyzed the blood flow dynamics in a stenosed, subject-specific, carotid bifurcation using the spectral element method. Somkid Amornsanmankul et al.[22] and Mamun Molla Md.[23] studied the pulsatile non-Newtonian flow of blood through stenotic artery. Srivastava et al.[24], Sapna Singh[25] investigated the effects of overlapping blood flow characteristics in a narrow artery. The simulation of complex dynamic processes that appear in nature or in industrial applications poses a lot of challenging mathematical problems, opening a long road from the basic problem, to the mathematical modelling, the numerical simulation, and finally to the interpretation of results.

In this paper, the axisymmetric viscous flow of a fluid in a stenosed vessel is considered. The blood gets thinner due to drug and density becomes lower leads to the freely motion of fluid inside the arteries. Under unsteady flow conditions the density variation is given as input. The work is undergone for mild (25%) and severe (90%) constrictions and different density variations (1060 kg/m^3 –normal, 1030 and 1000 kg/m^3 diluted) in a stenotic artery. The analysis of flow patterns was computed and compared using MATLAB and CFD. Limitations on constriction are ignored. The wall dispensability may be neglected since arterial wall is elastic.

2. Methods

2.1 Formulation of the Problem

The stenosed vessel was modeled using MATLAB Figure 1 and imported to CFD softwares for analysis.

The geometry of the stenosed vessel is given by

$$y(x)=\begin{cases} a\left(l-\dfrac{\delta}{2a}\left(l+\cos\left(\dfrac{\pi x}{x_0}\right)\right)\right), & |x|\le x_0 \\ a, & |x|, x_0 \end{cases} \qquad (1)^{19}$$

2.2 Boundary Conditions

On stenosed vessel, velocities u, v = 0

The velocity is calculated for the input pressure 12,000pa, u = 4.75831m/s, v = 0, as inlet.

Blood density ρ = 1060,1030, 1000 [kg/m^3] and dynamic viscosity η = 0.003 [kg/ms] (Poiseuille)

2.3 Governing Differential Equations

Equations of momentum and equation of continuity for an incompressible Newtonian fluid:

$$\nabla\cdot\vec{v}=0 \qquad (2)$$

$$\rho\left(\frac{\partial\vec{v}}{\partial t}+\vec{v}\cdot\nabla\vec{v}\right)=-\nabla p+\mu\nabla^2\vec{v} \qquad (3)$$

where: ρ - density of blood, $\vec{v}$ -velocity field, p - pressure, μ = co-efficient of viscosity.

2.4 Methodology

Computational fluid dynamics provides very detailed information about fluid characteristics. To study hemo-

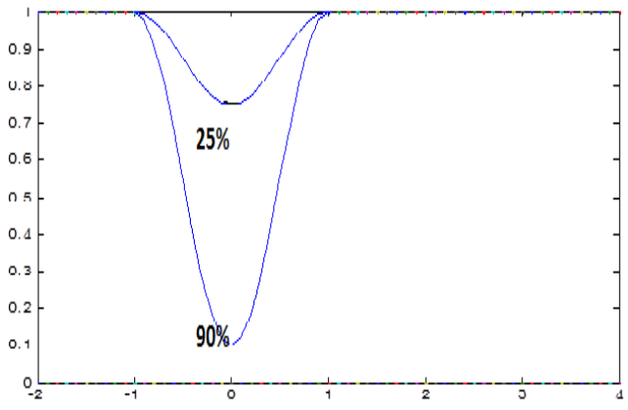

Figure 1. A Stenotic model with two constrictions

dynamic within the body medical science lent this new technology. CFD uses Finite Volume Method. A CFD solution involves the following basic steps:

i. Geometry creation.
ii. Choice of the models
iii. Apply of the boundary conditions
iv. Computation of flow field
v. Post processing

Formation, growth, and rupture of stenosis is easily understandable using CFD. This computational study analyses about velocity, pressure, and patterns of streamlines.

Discretization of the problem is done in Gambit. Equations were solved using finite volume method. There were no significant differences in the distribution of WSS, David[26] so in the simulation blood is considered as Newtonian. By solving 2 and 3 using the SIMPLE algorithm solutions were obtained.

3. Result and Discussion

By considering the domain Table 1, grid was generated with a pave mesh of size 0.01 was shown in Figure 2 and the nodal values are shown on Table 2. The volume and area statistics are shown in Table 3 and 4 respectively.

Unsteady flow at 10 time step size(s), for different time seconds 2, 4, 6, 8, 10 seconds for 1000 flow time, iterations were carried out and results are calculated.

Table 1. Domain of the geometry

	MIN.(mm)	MAX(mm)
X	–0.002	0.002
Y	0	0.001

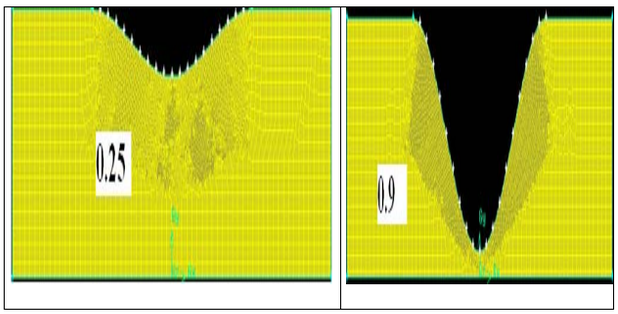

Figure 2. Pave mesh of size 0.01

Table 2. By considering interval size = 0.01, number of elements used in this model are

	0.25	0.9
Nodes	37998	31709
Mixed wall faces	808	878
Mixed press-outlet	100	100
Mixed press-inlet	100	100
Mixed interior faces	74482	61799
Quadrilateral cells	37493	31169

Table 3. Volume statistics

DIL.	Min. Volume (m3)	Max. Volume (m3)	Total volume (m3)
0.25	1.782426e-005	2.98966e-004	3.749941
0.90	3.453424e-005	1.855253e-004	3.099763

Table 4. Area statistics

DIL.	Min. Face area(m2)	Max. Face area(m2)
0.25	2.704820e-003	2.006518e-002
0.90	5.114161e-003	1.639324e-002

3.1 Velocity Magnitude

The velocity magnitude of unsteady flow with inlet velocity 4.75831m/s (12000pa = 90mmHg) for different densities are shown in Figure 3, and the minimum and maximum values are shown graphically in Figure 4 and streamline pattern are shown in Figure 6. Visualisation of fluid direction of velocity and velocity vectors are shown in Figure 3 and 5.

The normal blood density in human 1060 kg/m^3 is compared with the diluted densities 1000 kg/m^3 and 1030 kg/m^3. From Figure 3 and 4, the model with 90% stenosis has the lowest velocity 4.96m/s occurs for the density 1060 kg/m^3 and the high velocity 5.07m/s for density 1000 kg/m^3. For the model with 25% stenosis has the lowest velocity 5.54m/s for the density 1060 kg/m^3 and peak velocity 5.7m/s for density 1000 kg/m^3. The vortices and recirculation region shows the stagnation flow occurs in the downstream region of the constricted stenotic vessel. Figure 3 and 5 shows a very strong flow disruption and recirculation.

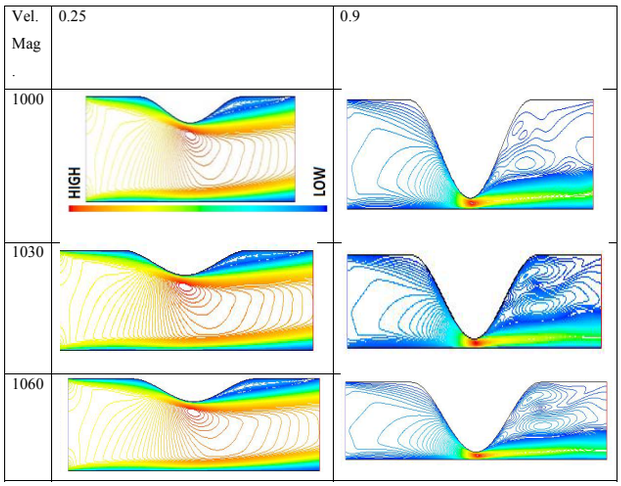

Figure 3. Contours of Velocity Magnitude

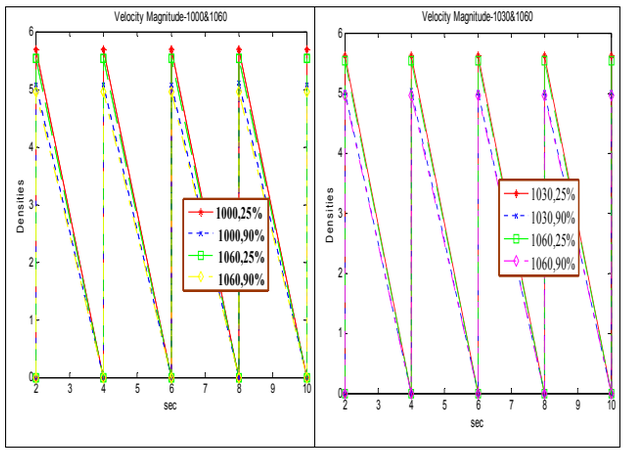

Figure 4. Graphical Representation of velocity magnitude.

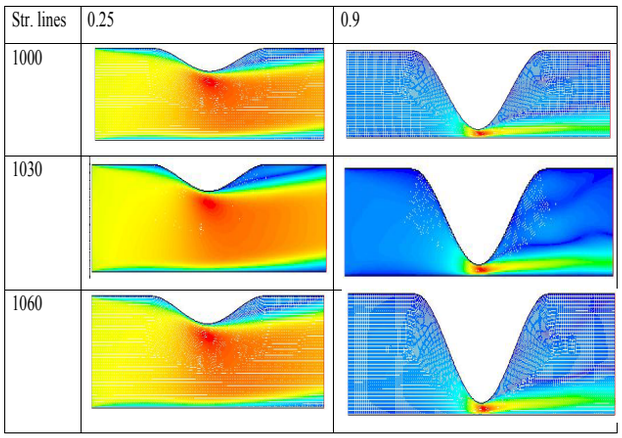

Figure 5. Contours of velocity vectors for velocity magnitude

3.2 Dynamic Pressure

According to the inlet pressure 12,000pa = 90mmHg for different models, dynamic pressure was calculated and shown in Figure 7, 8, 9.

Calculated pressures at different time seconds are shown in Figure 8 and streamline patterns are shown in Figure 9. The variability of pressures with increasing stenosis is shown in Figure 8. The pressure in the upstream region is dropped gradually in the downstream region. For model 25% constriction, the maximum pressure 121.97mmHg is shown at 2s for density 1060 kg/m^3 than others. Similarly for the model 90% constriction, the high pressure 97.73mmHg is seen at 2s for density 1060 kg/m^3 compared to others.

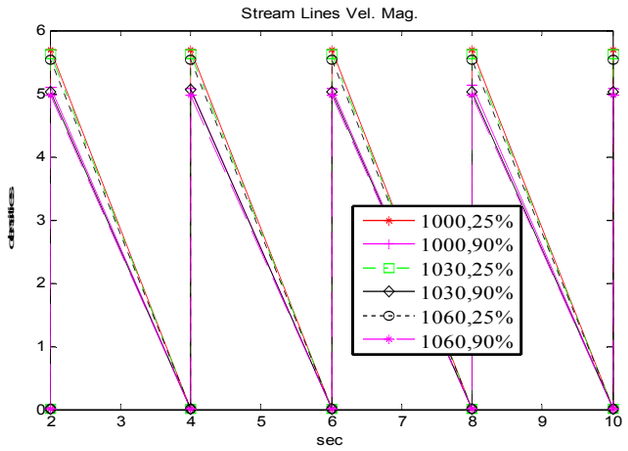

Figure 6. Streamline profile for velocity magnitude

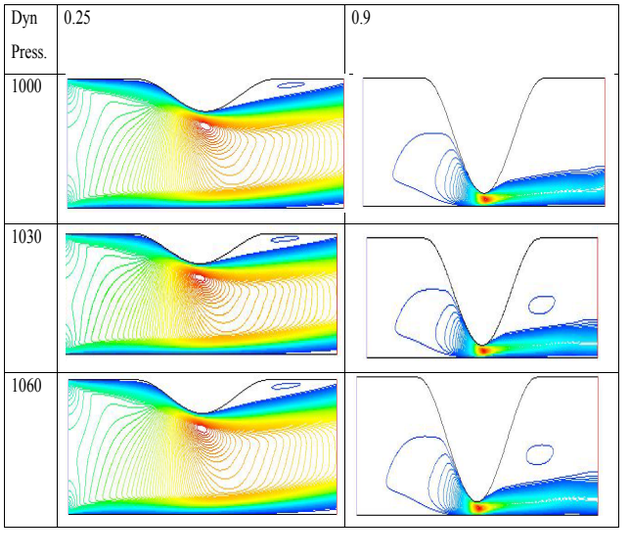

Figure 7. Contours of Dynamic Pressure

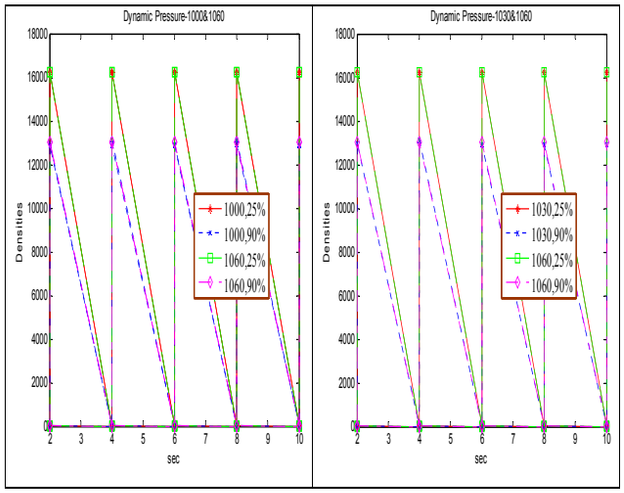

Figure 8. Graphical Representation of Dynamic Pressure

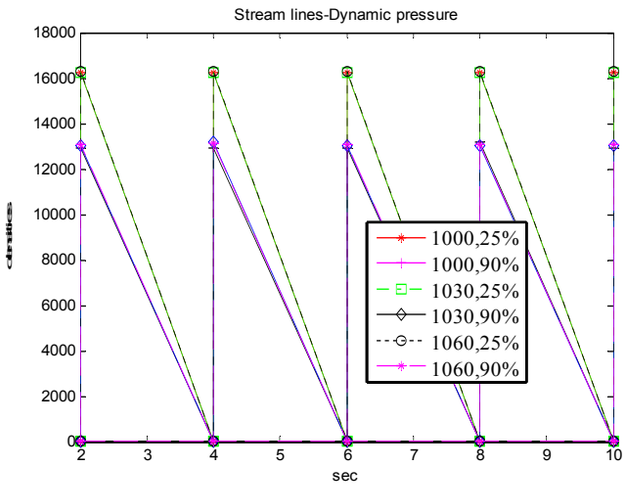

Figure 9. Streamline pattern of Dynamic Pressure

3.3 Wall Shear and Strain

The Wall shear and strain Figure 10 remain almost same up to 10 seconds, but decreases with increasing densities. Compared to 25% model, 90% have less shear stress at each time steps shown in Figure 11. For strain 90% are high compared to 25% and the ranges are graphically shown in Figure 12.

3.4 Convergence Map

The solution has been converges at different time steps. Equation of continuity, x and y momentum equations are converging correct to three decimal places and the results are shown in Figure 13.

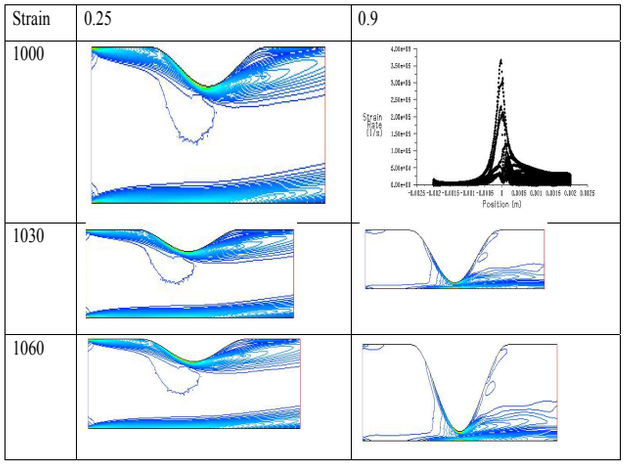

Figure 10. Contours of Wall Shear Stress and plot of Strain

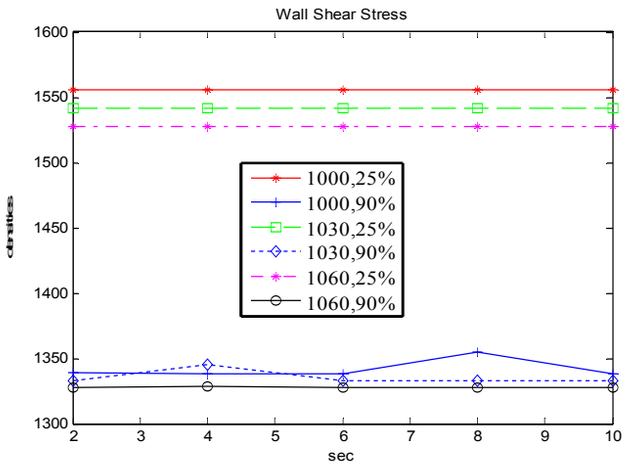

Figure 11. Graphical representation of wall shear

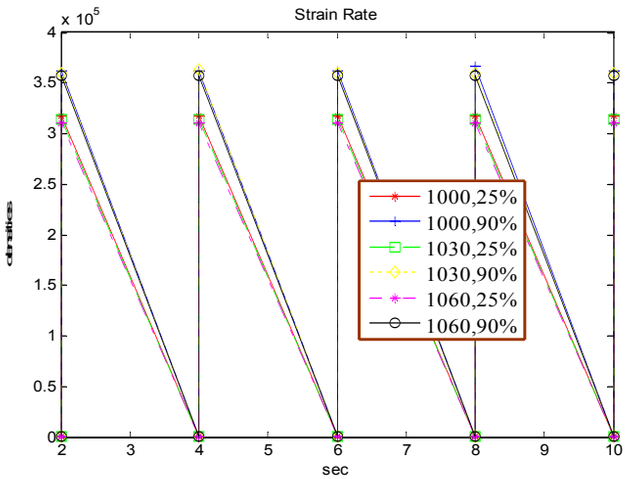

Figure 12. Graphical representation of strain

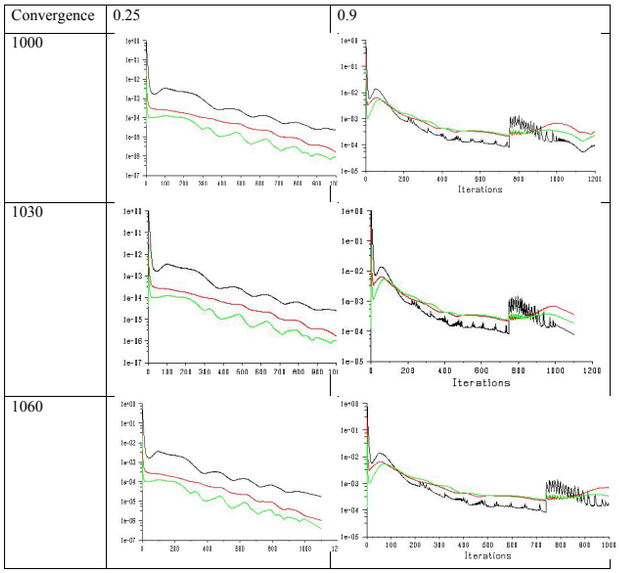

Figure 13. Convergence of governing differential equation

Flow analysis of the normal and diluted blood shows that an unsteady flow model is not similar for all stenoses. Flow characteristics are highly dependent on the geometry, different constriction of the vessels, flow densities and pressures. Low pressure and high velocity are obtained in the region of stenoses. The study based on computer flow are important to find the relationship between hemodynamic parameters and rupture. The formation of stenoses is the most dreadful biological reaction. Hence, complete understanding of the relationship between pressure, blood flow and symptoms for cardiovascular stenoses remains a critical problem. New devices to repair stenotic arteries are now being developed.

4. Conclusion

Aspirin prevents blood clots from forming inside arteries affected by atherosclerosis, but aspirin does not prevent atherosclerosis. Aspirin is readily available over the counter and thus is considered a 'safe' drug. Due to its antiplatelet action and fast acting aspirin is easy to use and safe at lower doses. Aspirin at moderate doses (160–325 mg/day) produces an antiplatelet effect rapidly (within 30 minutes). The medications of the interaction between aspirin and interactions with drugs: acetazolamide, corticosteroids, ibuprofen, probenecid, sodium valproate and warfarin varies depending upon the person taking them. By taking a number of NSAIDs at the same time the side effects can be cumulative. Prolonged use of aspirin at higher doses can cause stomach ulcers, and can also prolong bleeding. For those patients have already liver and kidney disease, this drug can impair function of the kidney and liver. Aspirin, non responders have higher rates of heart attacks, strokes, and death than aspirin responders. The causes of aspirin failure include inadequate dosing, not taking the medication regularly, concurrent intake of of other NSAIDs etc.

Medications and lifestyle changes are helpful to rectify from heart attack. Most people live many more years after their first attack and returned to their normal life. Most doctors recommend aspirin in healthy subjects who have one or more risk factors for developing atherosclerosis. Other measures are necessary to prevent atherosclerosis like losing excess weight, controlling HBP, diabetes, lowering LDL cholesterol, increasing HDL cholesterol and stopping cigarette smoking. Aspirin taken long-term is an important part, but NOT the only measure for preventing heart attacks. In the beginning stage we can take the salicylic acid in natural form as it is found in certain vegetables, fruits, nuts, seeds and herbs in various amounts. Future study will be based on the design of new devices that mimic the blood flow and predict flow of an individual.

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