INNOVATION AND IDEAS

Simulation Based Medical Treatment of Arteriosclerosis
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ABSTRACT
Objective: To study the usefulness of computer simulations in planning effective treatment of stenosed carotid arteries.
Study Design: Computational study of poststenotic areas of carotid arteries.
Place and Duration of Study: This study was carried out at the Department of Chemical Engineering, NED University of Engineering and Technology, Karachi from 15th April 2006 till date.
Materials and Methods: Geometric model of stenosed carotid artery with 75% stenosis was developed on Computational Software Gambit 2.0/Fluent 6.2 and important factors such as recirculations, low and high shear forces on wall, vortex formation etc. were analyzed, which are important to the formation and rupture of plaque.
Results: For 75% stenosis, it was found that in the post-stenotic region the recirculation existed suggesting increased area of low shear stress and thus further deposition of plaque. High shear forces were observed at the throat of stenoses indicating higher probability for plaque to rupture.
Conclusion: The preliminary results from computer simulations matched well with the in-vitro experimental data indicating that computer simulations could revolutionize the medical treatment of stenosed carotid arteries.

Key words: Arteriosclerosis. Haemodynamics. Computer simulations.

INTRODUCTION
The third leading cause of death and disability in the modern world is arteriosclerosis1-4 in which carotid artery supplying blood to brain is partially blocked due to deposition of fibrous material (plaque) and its rupture. It kills approximately 5 million people per year and is the major cause of adult neurological disability.5,6 About 80% of all strokes occur from vessel blockage with a significant proportion due to shedding of thromboemboli from atheromatous plaques in carotid stenoses into the brain.

To cure this arterial disease, surgeons use diagnostic methods such as ultrasound, Doppler, angiography, MRI and computed tomography to get anatomic and physiologic data. This is sometimes supplemented with physiologic data obtained from intravascular pressure and flow measurements. Empirical data is also collected to evaluate the efficacy of prior treatments for similar patients. Based on this data, several treatments are considered for instance medication, balloon angioplasty, stenting, surgery (endarterectomy), and bypass graft. However, above mentioned in-vivo diagnostic techniques usually do not yield sufficient data to help the surgeon in choosing the best medical treatment for the given patient. For example cases have been reported where restenosis occurred soon after angioplasty etc. Also the prediction of outcome of a given treatment remains difficult because of individual variability and inherent complexity of human biological systems. The chances of failure in short and long-term, therefore, exist.

A better approach to circumvent the above situation is to study pre- and post-treatment blood flow patterns (haemodynamics) as it is the prime cause behind the formation of plaque and its rupture. For instance, blood has same level of cholesterol everywhere in the body but arterial disease occurs only in certain areas such as carotid arteries, coronary arteries and abdominal aorta so definitely it has to do with haemodynamics. In carotid arteries, high shear force (drag force exerted by the blood on the artery wall) tends to break the plaque whereas low shear force causes deposition of plaque. Moreover, consideration of other haemodynamics parameters such as pressures, adverse flow conditions (back flow), flow recirculation, high temporal oscillations, and spatial gradients of shear stress, which promote thrombosis, arteriosclerosis and intimal thickening is also important.

With recent advances in Computational Fluid Dynamics (CFD) and modeling techniques as well as increased computing power, it has become possible to model blood flow more accurately (specially near fine artery wall where MRI and other techniques do not yield proper data) using parameters that closely resemble in-vivo conditions. Computational simulations for blood flow in arteries have been performed by many investigators for arteries with stenosis, curvature, bifurcations, graft and
In CFD, patient-specific arterial geometry is constructed from image data and fed to the computer with relevant modeling equations for flows. Fluid properties like density, viscosity, temperature as well as flow conditions are also incorporated. The geometry is divided into small cells or elements and the necessary boundary conditions are applied for pre- and postoperative condition. The simulation is then executed to extract information about important physiologic data that is otherwise not possible. A surgeon, therefore, has better idea to choose from various medical treatments.

The objective of this work was to incorporate latest mathematical equation for turbulence into CFD and compare its performance with in-vitro experimental data as well as to underscore the importance of CFD as a tool to assist surgeons in deciding treatment option for arteriosclerosis.

MATERIALS AND METHODS

In our preliminary work, we considered the experimental data of Deshpande and Giddens. Their experimental setup consisted of a 75% partially blocked smooth glass tube having a diameter of 0.508 m. The restriction was considered sinusoidal as is usually the case with plaque shape in the real carotid artery. Water with small percentage of ethylene glycol was chosen as a fluid to flow through the tube. A schematic of the stenosed geometry is shown below (Figure 1) in which the length of stenotic section was considered 2D where D is the diameter of the tube, the length of pre-stenotic section was taken 3D to impose fully developed flow and the length of poststenotic section was chosen 16 D to avoid difficulty in imposing downstream boundary conditions.

To simulate above experiments, a two dimensional (2D) steady state model was considered. The geometry was developed in Gambit 2.0, a pre-processor of main CFD Equations Solver Fluent 6.1. The domain was discretized into small elements, which were joined together at common points called nodes (Figure 2). It should be noted that the greater the number of nodes the more accurate the solution is but more CPU time and memory is also required. Thus, a compromise is sought by creating an optimum mesh before performing CFD simulations. The mesh so generated consisted of 47,500 quadrilateral cells. These cells were concentrated in the vicinity of the stenosis where flow gradients were expected to be high.

The governing equations of mass and momentum conservation were applied on the cells and solved numerically together with the boundary conditions such as no slip at the walls and known velocity and pressure at the inlet and outlet of the geometry respectively. Highly efficient numerical scheme was used to minimize the convergence errors. To capture the effect of turbulence, different well known models such as k-w and SST-kw were used. The CPU time to execute the simulation was recorded 10 minutes.

RESULTS

The plot of velocity contours are shown in Figure 3. The areas of high and low and even negative velocity and hence shear forces can be readily seen from the picture. The areas of low shear stress, recirculations and negative pressure are prone for plaque deposition whereas, high shear forces at the center of stenosis could rupture the plaque in real cases.

Narrowing an arterial lumen, or stenosis, tends to occur in regions of disturbed flow and low wall shear stress and once plaque develops and encroaches into the lumen, further flow disturbances are established. Haemodynamically, significant stenoses experience increased shear stress in the entrance region. In the post-stenotic region, the flow decelerates and tends to become unstable with separation, recirculation and generally for the more severe constrictions, transition to turbulence. Turbulence in blood flow influences a number of physiological parameters and processes among these are flow resistance, shear stress, pressure, mass transport from the blood to the vessel wall, wall remodeling, as well as platelet activation and aggregation. Of particular interest here are the effects of turbulence on mechanical forces acting on the stenosed vessel wall and its environment.

Low shear stress causes adverse changes in the
endothelium, including apoptosis, diminished nitric oxide synthesis and increased expression of adhesion molecules and chemotactic factors. Moreover, oscillatory strain and stress in the arterial wall stimulates responses including those that may also contribute to the progression of the disease. In later stages, recirculating flow and low oscillating shear may lead to inflammation and the production of matrix metalloproteinases, leading to matrix degradation. Platelets are sensitive to shear stress and levels of increased shear stress resulting from a stenosis have been shown to induce platelet activation and aggregation. Recirculating flow regions may also enhance delivery of activated platelets and monocytes to the arterial wall where longer residence time increases the likelihood of attachment. Thus, these changes promote thrombus formation in the poststenotic region, which is the likely site of embolus shedding. Thus, accurate estimation of shear stress in the region of interest is of prime importance.

Figure 4 shows the plot of shear stress (shear force per unit area) versus the axial distance of the tube. A comparison with the experimental work of Deshpande and Giddens at low Reynolds number of about 2000 (a parameter that characterizes the flow speed) is also included. The shear stress is highest at the center of stenosis (Z = 0, dimensionless distance) and falls rapidly in near poststenotic region to a negative shear stress region which indicates the existence of adverse flow (direction of flow is reversed). As it passes along the tube, the flow tends to stabilize so that positive shear stress is obtained at about Z=4. The point where adverse flow disappears is known as the reattachment point and the length from the center of stenosis to the reattachment point is called reattachment length. The accurate estimation of reattachment length is of significant importance since it gives the extent of stenosis severity in the artery. In case of large reattachment length more artery wall is susceptible to plaque formation and vice versa. Far from stenosis (after Z=4) the flow again become fully developed. The maximum shear stress was estimated to be about 58 N/m² which was not recorded by the experimental work. A slight discrepancy in experimental and model prediction is noted immediately after stenosis, apart from that, excellent match with experimental data was obtained. This is perhaps due to the inability of turbulence model used to capture flow transition from laminar to turbulence. We tried two well known turbulence model namely k-w and SST (Shear Stress Transport) but both predict similar behaviour in the area of concern. To circumvent this problem, other methods such as Large Eddy Simulation (LES) and Direct Numerical Simulation (DNS) have been presented in the literature but those are computationally very expensive.

It has been estimated that the blood flows through arteries at a Reynolds number of about 300 to 400 and when it passes through the restriction the Reynolds number could increase to above 1000. To simulate such a situation the model was compared with the experiments at Reynolds No. 1000 and excellent match was obtained as shown in Figure 5. The maximum shear stress estimated was 24 N/m². A slight deviation again exists close to the poststenotic region indicating that room exists to improve modeling equations.

DISCUSSION

The computer software successfully predicted important parameters for the development of arteriosclerosis such as shear stress, recirculation, adverse pressure gradients and vortex formations. Areas of low shear stress and extent of recirculation, which are prone to develop arteriosclerosis matched with high accuracy to those measured from experimental data. It should be noted that the prediction of velocities, very near to the wall, where MRI etc. are plagued by noise, were well estimated by CFD. Although experimental data collected used water as a fluid but exactly the same approach can be adopted for blood flow through arteries. This can be done by taking in-vivo data from real patients and feed that to the same model and simply changing the fluid properties from water to blood. This would be the next phase of this work.
In this preliminary work, a simplified case of 2D steady state model with smooth contours was considered. In reality, however, the blood flow is 3D pulsatile and hence unsteady. Moreover, the rigid wall condition is not applicable in real cases since artery walls are flexible. The incorporation of these phenomena would yield better predictions as to the development of plaque and its rupture.

Using this methodology, surgeons can plan and analyze treatment before entering the operation theatre. Thus, they would be able to identify those treatments that would result in best postoperative physiologic conditions. This would assist the understanding of the causes of strokes, heart attacks, and sudden cardiac death thus taking us closer to prevention. To support this statement an example of 75% stenosed carotid artery is presented.

Internationally, a good amount of research is going on to integrate computer simulations with medical planning. For instance, a clinical study is in progress in NHL1 St. Mary’s Hospital, Imperial College, to detect, via transcranial Doppler ultrasound, emboli in symptomatic patients with carotid stenosis, and tracking plaque per wall movement via motion analysis of B-mode ultrasound images. However, nothing has been done in Pakistan so far. It is, therefore, necessary for leading hospitals in Pakistan to come forward and support this kind of work for better health and safety of the nation.

CONCLUSION
The effectiveness of CFD simulations, to better understand flow conditions in stenosed vessels, is highlighted in this work. It is shown that CFD could help surgeons to choose the best medical treatment for arteriosclerosis.

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REFERENCES