JJMIE

Volume 13, Number 3, October. 2019
ISSN 1995-6665
Pages 141 - 148

Jordan Journal of Mechanical and Industrial Engineering

The Influence of Internal Carotid Artery Off-plane Angle on the Hemodynamics of Blood Flow in the Carotid Artery

Thakir AlMomani[*a], Suleiman Bani Hani[b], Othman Smadi[a], Salah Azghoul[a], Laila Kiswani[c], Majdoleen Assarsour[c]

[a]*Bioemdical Engineering department, Faculty of engineering, The Hashemite University, Zarqa, Jordan*
[b]*Mechatronics Engineering department, Faculty of engineering, The Hashemite University, Zarqa,Jordan*
[c]*The Hashemite University, Zarqa, Jordan*

Received 21 May. 2019

Abstract

The geometry of the carotid artery (IC) is thought to have a major role in causing blood flow related diseases in this artery. With age, different geometrical changes are observed to occur. These changes include: diameter, bifurcation angle, and internal carotid off-plane angle. The current study focuses on the changes that happen to the off-plane angle of the internal carotid artery to investigate the hemodynamic parameters that are thought to lead to the formation of plaques and atherosclerosis in this artery. Physiological values found in literature are used to compare vorticity and velocity fields for elderly and young people. Steady, three dimensional CFD computations were performed. Inlet velocity of 0.3 mm/sec, with no slip boundary conditions and rigid walls are used. The results showed that as the age or off-plane increases, the flow abnormalities and vorticity values increase. At the apex, the velocity values were the maximum near the inner wall, while at the mid and in the second half of the sinus, the velocity values were minimal and show back flow with higher values of vorticities. These results of the current study indicated that as the off-plane angle increases, as in elderly people, diseases of blood flow, such as atherosclerosis and unfavorable plaques, have higher probability to occur in such complicated artery.

Keywords: Carotid artery, aging, internal carotid off-plane angle, vorticity, velocity magnitude, atherosclerosis, plaques;

1. Introduction

Cardiovascular system is the system that is responsible for blood supply to different living tissues through blood circulation. Blood flow through this system is associated with many diseases that might cause insufficient blood supply, or lead to more complicated cases, such as strokes, heart attacks, and atherosclerosis. [(1)] Both experimental and numerical studies have shown that the initiation and the growth of cardiovascular diseases is not random. Regions with secondary flows, higher vorticities, and abnormal shear stress values are thought to promote more cell damage, deconstruction, and growth in the vessel lumen. [(1)]

One of the geometrical, critical, regions in the cardiovascular system is the carotid artery that provides brain and face with blood. The presence of the branching with the, normally, local dilation in the internal carotid artery (sinus) makes its geometry as one of the most complicated and favorable geometries that are thought to cause flow abnormalities that associated with atherogenic and atherosclerosis in this part of the arterial tree. [(1)]

1.1. Carotid Artery Related Diseases:

The preliminary stage of atherosclerosis and plaque formation is the presence of lipids in the vascular wall caused by sub endothelial retention of lipoproteins. High plasma concentrations of LDL-c (low-density lipoprotein cholesterol) and low plasma concentrations of HDL-c (high-density lipoprotein cholesterol) are each independent risk factors for the development of such diseases. [(2)] LDL has been shown to be the major carrier of cholesterol and the main atherogenic lipoprotein for atherosclerosis. In addition to concentrations of LDL and HDL in systemic circulation, some physical and fluid mechanical factors play an important role in the development of atherosclerotic plaques through the activation of blood constituents and endothelial cells. [(2)] The surface concentration of LDL is locally elevated in regions of fluctuated flow and fluctuated shear stress, which causes more flow abnormalities and provides a favorable condition for the formation of atherosclerosis and aggregated plaques. [(2)] Studies on flow dynamics in the carotid artery have demonstrated that laminar flow is

* Corresponding author e-mail: thakir2000@hu.edu.jo

disturbed at carotid bifurcation regions. The greatest plaque accumulation typically occurs on the outer wall of the proximal segment of the sinus of the internal carotid artery, in the region of the lowest wall shear stress. [1,2] The intimal thickness is the least on the flow divider side at the junction of the internal and external carotid arteries where wall stress is the highest. [3]

Experimentally, it was reported that atherosclerosis is the beginning of most of the diseases in brain that related to the blood flow, as more studies have demonstrated that occlusive thrombus triggered by plaque rupture is one of the major determinants of ischemic stroke in patients affected by carotid atherosclerotic disease. [4] The majority of ischemic strokes seem to result from embolization from an atherosclerotic plaque or acute occlusion of the carotid artery and propagation of the thrombus distally rather than static occlusion. The explanation for the low rate of total occlusions in carotid plaques is most likely related to high flow rates that limit thrombotic occlusions, unless there is severe luminal narrowing caused by repeated plaque ruptures. [5]

Due to the travelling parts of thrombus plaque from the carotid artery to the small arteries of the brain, which affects directly the hippocampus which is the part of the brain that is vital for learning and memory, particularly converting your short-term memory into long-term. [6] This part of the brain, also, helps human comprehend spatial relationships and navigate the world around him. Consequently, hippocampus is one of the first parts of the brain that suffers damage from plaques and tangles that light lead to Alzheimer's or paralysis diseases. Furthermore, clinical studies of the association of atherosclerosis risk factors and dementia have shown positive associations between dementia and carotid atherosclerosis. [6]

1.2. Flow Abnormalities in the Carotid Artery:

The unique geometry of the carotid artery has been correlated to the higher chances of formation of, mainly, atherosclerosis and the un-preferable plaques in this artery which might lead to strokes. As can be seen in figure 1, carotid artery combines branching, curvature, and blubbing (or dilation). All these geometrical complications cause to change the uniform, laminar flow upstream the apex into a turbulent - like, non-uniform flow downstream the internal and the external carotid arteries. [7] Such abnormalities are associated with abnormal shear stress values and higher vorticity values which will lead to cell deconstruction and proliferation. [8]

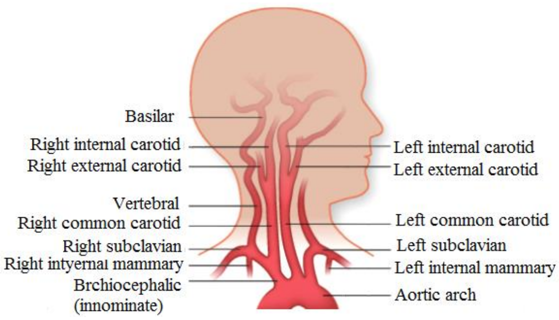


Figure 1. The geometry of the carotid artery

Vital cells as platelets, red blood cells, and endothelial cells are highly sensitive to the variation and abnormal fluctuations in the shear stress values. For example, Gnasso at el. (1996) have indicated the normal shear stress in human circulation is between 3.1 to 29.5dynes/cm^2. [9] In their study, Harish Shankaran at el (2002) have demonstrated that platelet activation occurs at 83 dynes/cm^2 value of shear stress. [10] Moreover, endothelial cells are used to be exposed to values of shear stress of 29.5 to 3.1 dynes/cm^2, higher or lower values of shear stress are, experimentally, observed to injure these cells, cause aggregation, growth, and proliferation new cells in the lumen of the blood vessel.[11, 12] More over, in the case of the negative pressure, recent experimental studies have indicated that these cells are showing higher trend to growth toward the internal of the artery lumen, causing the formation of un-preferable plaques in this area. [12]

On the other hand, experimental measurements of flow parameters, mainly shear stress and vorticities, in a scale of human carotid artery model have been conducted using different techniques such as: laser Doppler anemometry and MRI techniques. [13-18] The results of such studies are considered as a spark for many researchers to carry new in-vivo and in vitro experimental works or computational studies. In many cases, scientists tend to match experimental results with those that can be obtained from computational fluid dynamics simulations (CFD). [19,20] These recent studies aimed at defining the regions of high and low stress regions or the regions of diseases initiation.

As a result of these efforts, two theories have been adapted. The first one, which appeared early in 1960s, has mentioned that the main cell damage, deconstruction, and growth in the carotid artery resulted from the low shear stress values. [1] Based on their in vivo observations, and depending on different imaging techniques, they clearly found that more cells deposition and plaque formation is occurred on the external wall of the internal carotid artery. [1] Such regions are usually are associated with low shear stress values. Furthermore, they clearly stated that such low shear stress values are combined with both higher vorticities and negative pressure values. Such conditions are responsible to increase the residence and exposure time of the cells in such abnormal flow regime areas. [1]

Contradicting to the low shear stress theory, newer researchers performed more intensive in vitro experiments using flow regimes and geometries, similar to those that could be found in the physiological carotid artery. [1] In their results, they have mentioned that the cells are more sensitive to high shear stress values than lower shear stress values. More cell damage and deconstruction were observed to occur in the apex of the internal carotid artery, where higher blood streams and shear stress values are observed. Based on that, they conclude that diseases in the carotid artery are initially appeared in the high shear stress values then it develops there. [1]

In the last two decades, these two theories were studied intensively. More concern and attention were given to the low shear stress theory. Many researchers have reported that accumulative effect of flow abnormalities on both blood constituents and endothelial cells is more critical than the instantaneous effect of abnormal values. Cells need to stay for a certain and longer time to get activated and start to from clots and plaques. The presence of vorticities causes them to be exposed more to the abnormal flow values, and hence abnormal growth in such areas. (21)

One of the major geometrical issues that has been reported to affect the flow abnormalities in the carotid artery is the bifurcation angle between the internal and the external carotid arteries and the plane off angle. In their work, Thomas et al. (2005) and Jeon et al. (2017) accomplished a statistical study between the old and young people to investigate the differences between the geometry of the carotid artery between young and old people using MRI imaging technique. (4, 21) In their findings, they show that young people have, almost, uniform shape with little or no curvature in their carotid artery. While old people, they reported that carotid artery has a non-uniform with curvature rates occur in the internal carotid artery. (21) In numbers, they mentioned that the bifurcation angle for young people has an average of 48.5^o people while it has an average value of 63.6 o for elderly people. On the other hand, they reported that the plane off angle for young people is almost 0^o while it's around 16^o for elderly ones. These variation in shape between the young's and elders' carotid artery may be related to the reason why the cerebral vascular accident occurrence in the elder has higher probability than young. (4, 21)

1.3. Objectives

The current work utilized CFD simulations to investigate the influence of off-plane angle variation on the flow parameters of the fluid, mainly velocity and vorticity fields. Off-plane angles of 0^o, 5^o, 10^o, and 15^o will be used. More focus will be given to the flow patterns in the sinus of the internal artery. As mentioned earlier this normal dilatation is thought to be the most critical place where more brain diseases start at. Computational models are built based on the geometries found in literature. (4, 21) FLUENT-ANSYS software is used to create the mesh, identify boundary and initial conditions, and solve flow equations.

2. Methodology

2.1. Geometry and Dimensions

Dimension and geometries reported in Thomas Et al. 2005 is used to construct the current geometry. The dimensions are shown below in table 1. As mentioned earlier the off-plane angles are 0^o, 5^o, 10^o, and 15^o as shown in figure (2). (4, 22)

Table 1. Dimension of simulated carotid artery

Parameter	Diameter (mm)	Length (mm)
CCA Diameter	8	47
ICA Diameter	5.5536	60
ECA Diameter	4.6224	60
major Sinus	22	
minor Sinus	8	

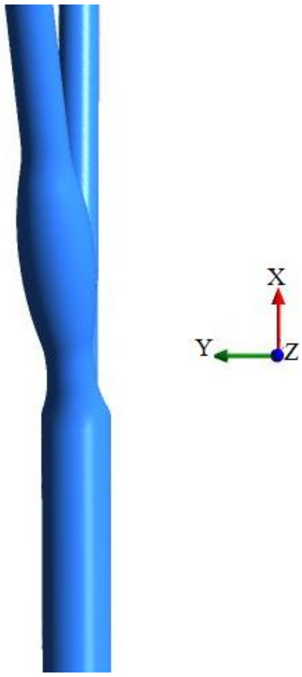


Figure 2. Model of the used carotid artery that shows the off-plane angle.

2.2. Governing equations, boundary, and initial conditions:

The governing equations include the incompressible equations of mass and momentum conservation given by:

$$\frac{\partial u_x}{\partial x}+\frac{\partial u_y}{\partial y}=0 \quad (1)$$

$$\rho\left(\frac{\partial u_x}{\partial t}+u_x\frac{\partial u_x}{\partial x}+u_y\frac{\partial u_y}{\partial y}+u_z\frac{\partial u_z}{\partial z}\right)= -\frac{\partial P}{\partial x}+\mu\left(\frac{\partial^2 u_x}{\partial x^2}+\frac{\partial^2 u_y}{\partial y^2}+\frac{\partial^2 u_z}{\partial z^2}\right) \quad (2)$$

Here, u_x, u_y,and u_z are the velocity along, x, y, and z-directions. ρ is the blood density, μ is the blood viscosity.

For the boundary conditions, the vessel walls are prescribed as rigid walls with no slip boundary condition. At the inlet, the velocity specified to be 0.3mm/s. At the outlet, the standard outflow condition is applied, i.e., the velocities are linearly extrapolated and corrected to be consistent with global mass conservation and a Neumann condition is applied on the pressure. The blood is treated as non-Newtonian homogenous fluid with density of 1060 kg/m^3 and a viscosity of 0.0035 kg/m.s.(1) The iterative technique is used to solve the above equations with initial velocity vector of zero magnitude.

3. Computational method:

Flow in carotid artery is simulated using finite volume-based software package ANSYS-FLUENT. The mesh is constructed using pro-E software. Different off-plane angles were used to simulate the flow in elderly and young carotid arteries. Figure 3 shows the velocity magnitude plotted versus radial location at the inlet of the sinus region for different mesh sizes for an off-plane angle of 0^o. Grid independency was performed for many cell numbers starting with 353209 and ending with 583139, the magnitude of the velocity magnitude is presented versus the radial location of the centre plane of the carotid sinus. As can be observed on this figure grid independency occurred when the cell number was 436261. Consequently, this mesh size is used for the rest of the simulations.

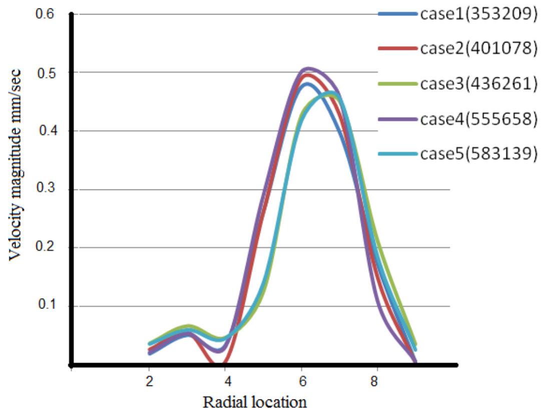


Figure 3. Mesh independency; velocity magnitude versus radial position in the mid of the sinus plane.

4. Computational Results:

Four different IC off-plane angles have been simulated and analyzed to study the influence of aging with the hemodynamics of blood and carotid bifurcation. Physiological flow conditions are applied for all cases. The results are mainly include the velocity and vorticity contours for different planes; three of them present the sinus region, and one plane is the medial plane that perpendicular on the IC such that this plane divided the IC carotid artery into two symmetric volumes, so that the internal and external walls of the IC artery are captured in this plane (figure 4). Consequently, the flow changes in the inner and the outer walls of the sinus cane be clearly demonstrated.

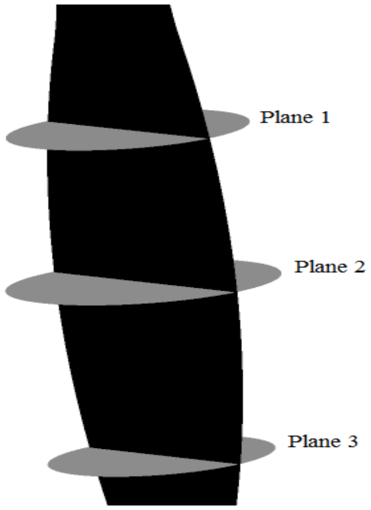


Figure 4. Presented planes to show simulated results.

4.1. Velocity contours

Figures (5-7) shows the contours of the velocity magnitude, for the studied off-plane angles for locations number 1, 2, and 3 (as numbered and shown on figure 4). For all cases, at the outer IC wall, velocity magnitude became lower and lower, while at the internal wall of the IC the velocity magnitude became higher and higher. Also, in all cases velocity gradient, and hence shear stress, is changed as off-plane angle increases.

Figure 8 shows the velocity contours for the frontal plane of the carotid artery. Also, in this figure, values of velocity are dependent on the off-plane angle. The minimal velocity values occurred on the outer wall region and decrease with increasing the off-plane angle, while maximal values occurred near the inner walls and increase with increasing the off-plane angle. In addition to the inner and the outer walls, this figure shows the maximum velocity value and magnitude occurs at the division between the internal and the external arteries, i.e., the apex of the carotid arteries. As can be seen in the figure, the blood stream became higher and greater downstream the apex or the bifurcation angle as the off-plane angle increases.

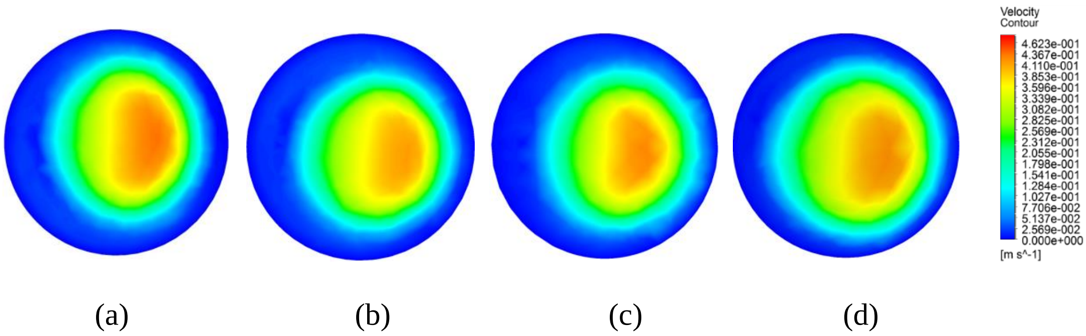


Figure 5. Velocity contours (plane 3: start of the sinus); off-plane angle of: a) 0^o b) 5^o c) 10^o d) 15^o

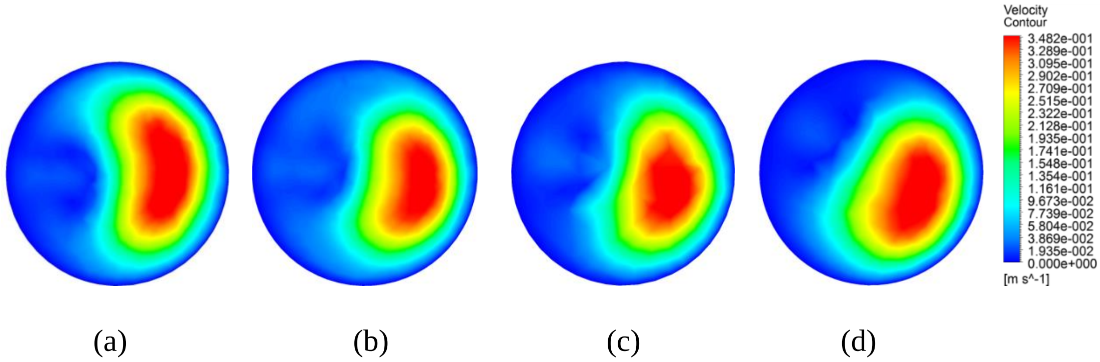


Figure 6. Velocity contours (plane 2: Mid of the sinus); off-plane angle of: a) 0^o b) 5^o c) 10^o d) 15^o

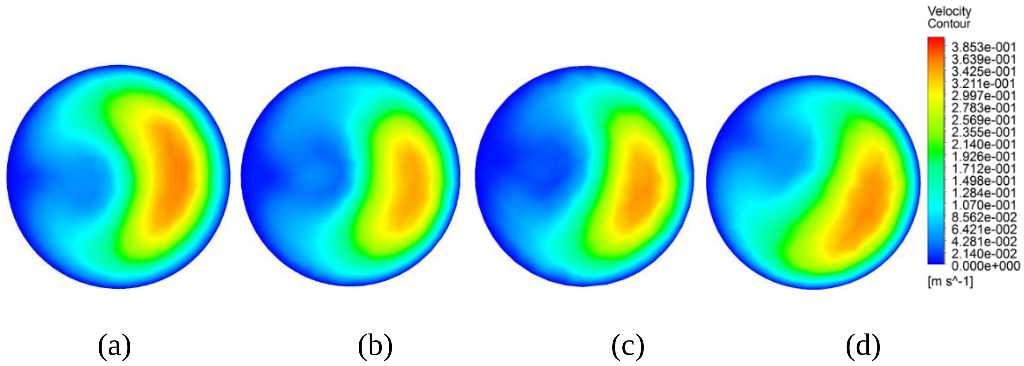


Figure 7. Velocity contours (plane 1: end of the sinus); off-plane angle of: a) 0^o b) 5^o c) 10^o d) 15^o

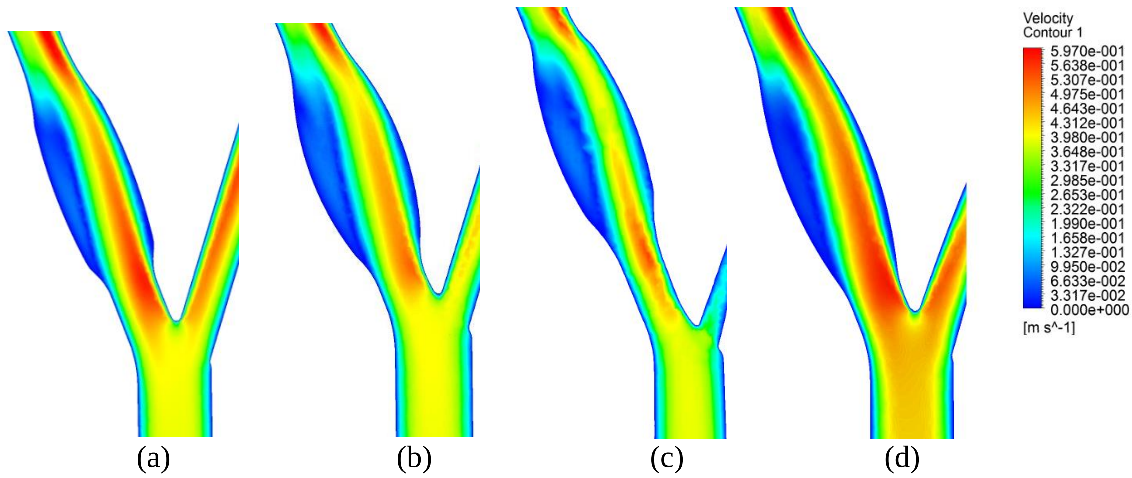
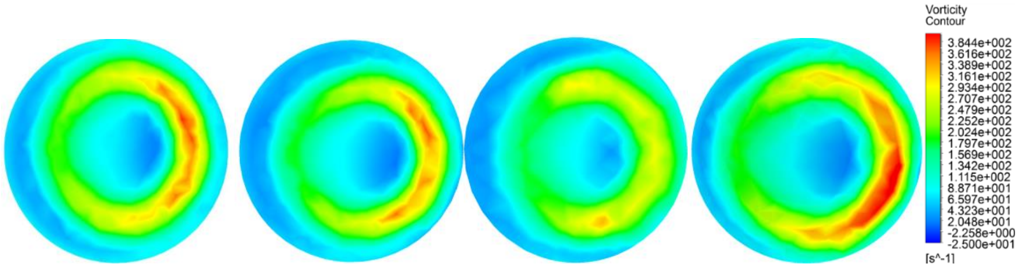


Figure 8. Velocity contours in the medial plane of the sinus with off-plane angle of: a) 0^o b) 5^o c) 10^o d) 15^o

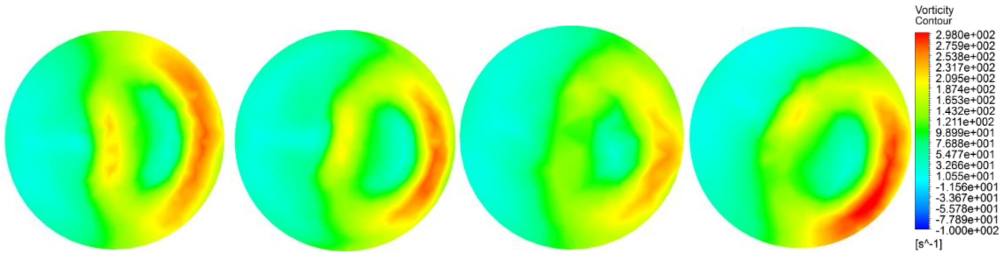
4.2. Vorticity contours:

To study flow abnormalities, vorticity contours are plotted for different angles, different planes (figures 9-12).in all cases, it's clearly observed that aging is causing strong changes in vorticity values. In all sinus planes, the vorticity became maximal on the internal wall and minimal on the outer walls. These values are clearly changed with the off-plane angle. The greatest changing can be observed in figure 11 that represents the second half of the sinus. To get more comprehensive picture, the vorticity contours are plotted for different angles on the frontal plane of the carotid artery (figure 12). The results of this figure show the trend of increasing the vorticity values near the internal wall, and the decreasing of these values near the outer wall. According to literature the accumulative effect of the elevated vorticity values is thought to have a major influence in the disease initiation in the sinus of the carotid artery. Lower vorticity values are indication of the longer residence time for blood constituents, like platelets and LDL, that consider the primary cells that are responsible for plaque formation. Also, the long residence of the LDL can be correlated to the injuries that could happen in the endothelial cells.



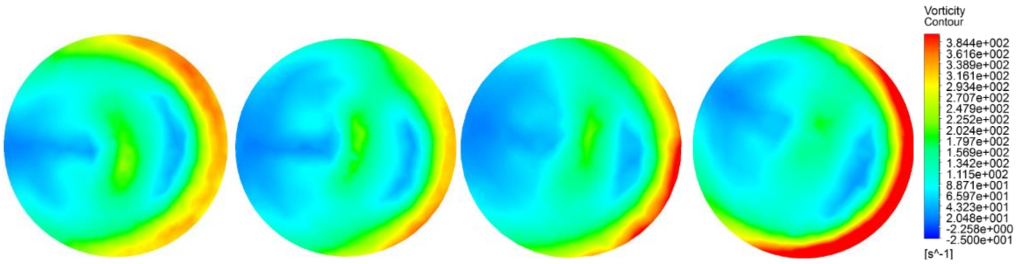
(a) (b) (c) (d)

Figure 9. Vorticity contours (plane 3: start of the sinus); off-plane angle of : a) 0^o b) 5^o c) 10^o d) 15^o



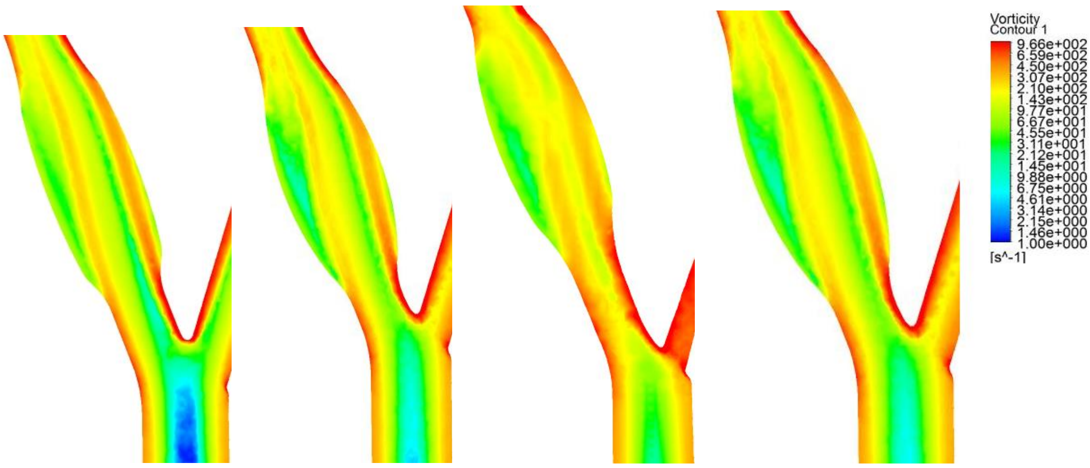
(a) (b) (c) (d)

Figure 10. Vorticity contours (plane 2: start of the sinus); off-plane angle of: a) 0^o b) 5^o c) 10^o d) 15^o



(a) (b) (c) (d)

Figure 11. Vorticity contours (plane 1: start of the sinus); off-plane angle of : a) 0^o b) 5^o c) 10^o d) 15^o



(a) (b) (c) (d)

Figure 12. Vorticity contours in the medial plane of the sinus with off-plane angle of: a) 0^o b) 5^o c) 10^o d) 15^o

5. Discussion

Previous statistical studies are concluded that the coincidence of atherosclerosis, thermogenesis, and strokes is higher for elderly than younger people. Different reasons were reported as biological factors, stress factors, smoking, genetics, and mechanical factors. As the current results indicated, the unique geometry of the carotid artery is thought to be one of the key players that has major role in promoting mechanical factors that lead to the initiation of such diseases.[23] The effect of the geometry is, actually, due the direct changes that happen to the flow stream in this artery. As well known, blood related diseases are not random in the cardiovascular system. The areas with branching, curvature, and sudden area changes are more promoted to cause and create abnormal flow regimes that have direct effect on the vital cells either in the blood itself or the vessel wall.

According to previous experimental works that they used different image techniques, as the human being getting older and older three major changes can be observed in the geometry of the carotid artery; first, the radius of the common and the internal carotid arteries increases with age. Second, is that the bifurcation angle between the internal and the external carotid artery is also increasing with age. Finally, the off-plane angle of the internal carotid artery increases with age.

The current work is employed the CFD computations to study the higher coincidence of brain-blood hemodynamic diseases with aging. More focus is given to the off-plane angle of the IC. As what was expected, the results of this work improved that the normal changes in the off-plane angle leads to create more flow abnormalities with higher values. The presence of higher velocity blood stream near the apex, means higher shear stresses there, vital cells, mainly platelets and endothelial cells, are highly sensitive to such values. Consequently, the formation of abnormal plaques and atherosclerosis in such region.

In the sinus region, the formation of secondary flows and vorticities is observed for all cases, this formation is associated with separation and higher recirculation. All these abnormalities are getting higher and higher with increasing of the off-plane angle. Adjacent to the outer wall of the sinus, such flow patterns are thought to cause LDL, platelets, and other blood constituents to stay there for longer time. Thus, the exposure of such cells to abnormal shear values will cause them to get promoted, activated, and hence the formation un-preferable plaques there.

Post the formation of plaques and atherosclerosis in different regions in the carotid artery, the higher blood stream near the centerline of the sinus might cause fragmenting of small parts of the plaque. Consequently, dragging and moving small masses of lipids or other cells along with the main blood stream toward cerebral arteries in different places on the brain. Post of the sinus, the internal carotid artery will branch into smaller arterioles with small diameters. As the fragmented mass reaches smaller diameter arteriole, than its dimension, it will block this arteriole and, might cause stroke.

6. Conclusions

The current work showed that the flow complexity increases in older people who have higher internal carotid off-plane angle values. Consequently, higher probability of the formation of atherosclerosis or plaques in the sinus of the carotid artery and hence brain strokes. Referring to literature, the results of the current study showed good agreement with most of the previous experimental and computational studies that have been accomplished to date. Despite of that, more work is still needed to find a comprehensive model and understanding the mechanism of plaque formation under physiological conditions.

Finally, this study evoked many assumptions. For example, all walls were treated as rigid, the blood is treated as homogenous Newtonian fluid, and the flow regime is assumed to be laminar steady flow. In physiological conditions, the wall artery is distensible and react with blood wave through dilation and constriction. Moreover, the flow in the carotid artery is unsteady pulsatile and not steady. Thus, more studies are still needed to mimic the physiological flow regime with its values in the carotid artery.

7. Declarations

7.1. Ethical Approval and Consent to participate

The present paper does not report on or involve the use of any animal or human data or tissue

7.2. Consent for publication

The present paper does not contain data from any other works

7.3. Availability of supporting data

The data and results used and/or analyzed during the current study are available from the corresponding author on reasonable request

7.4. Competing interests

The authors declare that they have no competing interests

7.5. Acknowledgements

We would like to acknowledge The Hashemite University for its support.

7.6. Funding

This work is partially funded by the Hashemite University / Jordan.

7.7. Authors' contributions

T. A., L. K., and M. S, performed computational studies. T.A., wrote the manuscript, S. B., O.S., and S. A. revised figures, read, and approved the final manuscript.

7.8. Authors' information

None

References

[1] Chandran KB, Rittgers SE, Yoganathan, Biofluid Mechanics: The Human Circulation. CRC/Taylor & Francis: Boca Raton, 2007; 419.

[2] AlMomani T, UdayKumar H S, Marshall J S, and Chandran K B. Micro-scale Dynamic Simulation of Erythrocyte–Platelet Interaction in Blood Flow. Annals of Biomedical Engineering. 2008; 36: 905–920.

[3] Gijsen FJ1, van de Vosse FN, Janssen JD. The influence of the non-Newtonian properties of blood on the flow in large arteries: steady flow in a carotid bifurcation model. J Biomech. 1999; 32(6); 601-608.

[4] Thomas B. J, Antiga L., Susan L., Jaques S., Steinman D.A. H., Spence D., Rutt B. K., Variation in the Carotid Bifurcation Geometry of Young Versus Older Adults Implications for Geometric Risk of Atherosclerosis. Stroke. 2005; 36; 2450-2456.

[5] Samuel KC. Atherosclerosis and occlusion of the internal carotid artery. J Path Bact. LXXI. 1956; 391-401.

[6] Susan K Roepke, Elizabeth A Chattillion, Roland von Känel, Matthew Allison, Michael G Ziegler, Joel E Dimsdale, Paul J Mills Thomas L Patterson, Sonia Ancoli-Israel, Susan Calleran, Alexandrea L Harmell, and Igor Grant. Carotid plaque in Alzheimer caregivers and the role of sympatho-adrenal arousal. NIH public access. 2011; 73(2); 206-213.

[7] Chistiakov DA1, Orekhov AN, Bobryshev YV. Effects of shear stress on endothelial cells: go with the flow. Acta Physiol (Oxf). 2017 Feb;219(2):382-408.

[8] Federico Vozzi, Jonica Campolo, Lorena Cozzi, GianfrancoPolitano, Stefano Di Carlo, Michela Rial, Claudio Domenici, and Oberdan Parodi. Computing of Low Shear Stress-Driven Endothelial Gene Network Involved in Early Stages of Atherosclerotic Process. BioMed Research International. Sep 2018; 2018: 1-12.

[9] Gnasso A, Carallo C, Irace C, Spagnuolo V, De Novara G, Mattioli PL, Pujia A. Association between Intima-Media Thickness and Wall Shear Stress in Common Carotid Arteries in Healthy Male Subjects. Circulation. 94(12):3257-62.

[10] Shankaran H, Alexandridis P, Neelamegham S. Aspects of hydrodynamic shear regulating shear-induced platelet activation and self-association of von Will brand factor in suspension. Blood. 2002; 101(7):2637-45.

[11] Zhanjun MA, Kangquan S, Zonghuan LI, Chao I, Baiwen QI, Aixi YU. Negative pressure wound therapy promotes vessel destabilization and maturation at various stages of wound healing and thus influences wound prognosis. Exp Ther Med. 2016 Apr; 11(4): 1307–1317.

[12] Ming Chen, Baohua Huang, Fang Yang, Wei Shu, Zhenfeng Chen, Ming Chen. Functional Roles of Shear Stress in Vascular Endothelial Cells. Cellular Immunology and Serum Biology. 2017; 3(1):64-67.

[13] Zarins CK, Giddens DP, Balasubramianan K, Sottiurai V, Mabon RF, Glagov S. Carotid plaques localize in regions of low flow velocity and shear stress. Circulation. 1981; 64:44.

[14] Perktold K1, Resch M, Florian H. Pulsatile non-Newtonian flow characteristics in a three-dimensional human carotid bifurcation model. J Biomech Eng. 1991 Nov; 113(4):464-75.

[15] Karino T, Goldsmith HL. Flow behavior of blood cells and rigid spheres in an annular vortex. Philos Trans Roy Soc Lond B Biol Sci. 1977 Jun 10; 279(967):413-45.

[16] Stokholm R, Oyre S, Ringgaard S, Flaagoy H, Paaske W.P, Pedersen E.M. Determination of wall shear rate in the human carotid artery by magnetic resonance techniques. European Journal of Vascular and Endovascular Surgery 2000 Nov; 20(5):427-33.

[17] Fayad Z.A, Fuster V. The human high-risk plaque and its detection by magnetic resonance imaging. American Journal of Cardiology. 2001; 88(2A):42E-45E.

[18] Marshall I, Papathanasopoulou P, Wartolowska K. Carotid flow rates and flow division at the bifurcation in healthy volunteers. Physiological Measurement.2004; 25 (3): 691–697.

[19] Papathanasopoulou P, Zhao S, Kohler U, Robertson M.B, Long Q, Hoskins P, Xu X.Y, Marshall I. MRI measurement of time resolved wall shear stress vectors in a carotid bifurcation model, and comparison with CFD predictions. Journal of Magnetic Resonance Imaging. 2003; 17: 153–162.

[20] Younis H.F, Kaazempur-Mofrad M.R, Chan R.C, Isasi A.G, Hinton D.P, Chau A.H, Kim L.A, Kamm R.D. Hemodynamics and wall mechanics in human carotid bifurcation and its consequences for atherogenesis: investigation of inter-individual variation. Biomechanics and Modeling in Mechanobiology. 2004; 3 (1):17–32.

[21] Se Jeong Jeon, Hyo Sung Kwak, and Gyung Ho Chung. Widening and Rotation of Carotid Artery with Age: Geometric Approach. J Stroke Cerebrovasc Dis. 2018 Apr 19; 27(4):865-870.

[22] David N. Ku, Don P. Giddens, Christopher K. Zarins, and Seymour Glagov. Pulsatile Flow and Atherosclerosis in the Human Carotid Bifurcation Positive Correlation between Plaque Location and Low and Oscillating Shear Stress. Arteriosclerosis. 1985; 5 (3): 293-302.

[23] Estelle E. Seyman, Natan Bornstein, Eitan Auriel, Oren Cohen, Tania Nissel & Hen. Hallevi. Assessment of carotid artery ultrasonography in the presence of an acoustic shadow artifact. BMC Neurology 2019; 19: 178 – 186.