Effect of Microvessels Stiffness on Hemodynamic; an FSI Analysis

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Abstract

The exploitation of computer modelling in the study of cardiovascular disease has recently gained significant progress. In this study, the effect of microvessels stiffness on blood pressure and blood flow-induced wall shear stress (WSS) was analysed numerically. Three microvessels with diameters of 100, 200 and 300 microns and respectively media thicknesses of 10, 20 and 30 microns, were designed. Then for each model, three different elastic moduli of 0.4, 0.6 and 0.8 MPa were assigned. The blood flow within the microvessels was investigated using CFD analysis. A fluid-structure interaction (FSI) multiphysics analysis was performed to observe the effect of vascular stiffness on blood pressure and vice versa the effect of blood flow on the microvessel deformation. The result of the analysis showed that increasing the stiffness of a vessel increases blood pressure and WSS, and as well as causes a decrease in its deformability. The outcomes of this theoretical study shed more light on the understanding of cardiovascular diseases roots and origin, especially in micron-sized vessels..

Keywords: Hypertension, Wall shear stress, Vessel stiffness, FSI analysis, CFD analysis

Mikrodamarların Sertliğinin Hemodinamik Üzerine Etkisi; bir FSİ Analizi

Öz

Kardiyovasküler hastalıkların araştırmasında bilgisayarla modelleme son zamanlarda önemli ilerleme kaydetmiştir. Bu çalışmada; mikrodamar sertliğinin kan basıncı ve kan akışından kaynaklanan çeper kayma gerilmesi (WSS) üzerindeki etkisi, sayısal yöntemle analiz edilmiştir. Çalışmada üç mikrodamar tasarlanmıştır. Tasarlanan bu üç mikrodamar 100, 200 ve 300 mikron çaplarında ve sırasıyla 10, 20 ve 30 mikron kalınlıkta tasarlanmıştır. Daha sonra her mikrodamar için malzeme özelliği olarak 0.4, 0.6 ve 0.8 MPa'lık üç farklı elastisite modülü uygulanmıştır. Mikrodamarlarda ki kan akışı, CFD yöntemi ile analiz edilmiştir. Damar sertliğindeki değişimin kanın uyguladığı basınç üzerindeki etkisini ve ayrıca kan akışının damarın deformasyonu üzerindeki etkisini incelemek için bir sıvı-yapı etkileşimli (FSI) analizi gerçekleştirilmiştir. Analizler sonucunda: Damar sertliğinin artmasının kan basıncını ve WSS'i artırdığını ayrıca mikrodamarın deformasyon kabiliyetini düşürdüğünü göstermiştir. Bu çalışmanın sonuçları, kardiyovasküler hastalıkların özellikle mikron boyutlu damarlarda incelenmelerine ışık tutmuştur.

Anahtar Kelimeler: Hipertansiyon, Çeper kayma gerilmesi, Damar sertliği, FSI analizi, CFD analizi.

1. Introduction

Cardiovascular disease (CVD) is the leading cause of death in the world, as a study showed that a quarter of deaths was due to CVDs in 2010 (Lozano et al., 2012).

Numerous factors, including nutrition (Casas, Castro-Barquero, Estruch, & Sacanella, 2018), sleep duration (Ren et al., 2018), genetic background (Borén et al., 2020), air pollution (Miller & Newby, 2019) contribute to CVDs. CVDs can be classified in main groups like atherosclerotic, cerebrovascular disease, venous thromboembolism, peripheral vascular disease, myocardial infarction and cardiac arrhythmias or stroke (Flora & Nayak, 2019). Any CVD has a special characteristic and should be studied in an exclusive pathology. In severe CVDs cases, blood flow within vascular reduces or completely stops. Blood flow reduction or stopping within an artery is the consequence of its blockage or rupture. Blood blockage in coronary arteries can lead to a heart attack or stent implantation (Dash, 2013). But in the case of vessel wall rupture and bleeding in vital organs like brain, it can damage the surrounding tissues (Katt, Linville, Mayo, Xu, & Searson, 2018).

Despite tremendous advances in the diagnosis and treatment of CVDs, the real roots and mechanisms of rupture or blockage of blood vessels are still less understood (Markwald, Norris, Moreno-Rodriguez, & Levine, 2010). Understanding factors, background and mechanism that contribute to this kind of diseases, can lead us to find solutions and treatment strategies to reduce and control mortality rate in CVDs.

Many studies suggest that always there is a correlation between blood pressure and CVDs (Yamagishi, Sawachi, Tamakoshi, Iso, & Group, 2019), (Wu et al., 2015), (Franklin & Wong, 2013). For example, O'Donnell, M.J., et al. in a statistical study showed that a reduction in blood pressure can reduce ischemic and intracerebral hemorrhagic stroke (O'Donnell et al., 2010). In a similar study Rapsomaniki, E., et al., showed people with a systolic blood pressure of 90–114 mm Hg and diastolic blood pressure of 60–74 mm Hg are in the lower CVDs risks compared to those with higher blood pressure

(Rapsomaniki et al., 2014). Therefore, clarifying the causes of hypertension looks to be the first step in CVDs studies (Wu et al., 2015), (Fuchs & Whelton, 2020).

Blood pressure physically can be explained as the exerted force by blood on a vessel wall area and, this is why the blood pressure phenomenon is investigated using hydrodynamic principles (Yoganathan, Cape, Sung, Williams, & Jimoh, 1988). Since blood flow occurs within a flexible vessel, the physical properties of both blood and vessel structure are expected to be effective in blood hemodynamics and exerted stress on the vessel wall (Wang, Quaini, & Canic, 2018). In this regard, computer modelling in hemodynamic analysis, parallel to experimental studies gained more attention in recent years (Vardhan et al., 2019),(Lipp et al., 2020), (Mittal et al., 2016). For example, Simone et al. study showed increases in blood viscosity contribute to high blood pressure (de Simone et al., 2005). Given that, experimental studies require expensive equipment and a great deal of data, computer modelling, with all its limitations, seems to be a powerful tool in hemodynamics studies (Zhang et al., 2014). For instance, the author's previous work showed that higher blood viscosity in a stenosed artery could significantly change pressure and wall shear stress on the vessel wall (Ali & Önel, 2018). Hoi Y et al. showed the result of computational fluid dynamics (CFD) analysis of the effect of the geometric variation on cerebral aneurysms was very good agreement with particle image velocimetry technique analysis result (Hoi, Woodward, Kim, Taulbee, & Meng, 2006). The handicap of the recent two studies is that the vessel wall was assumed as a rigid body. But blood pulsatile causes deformation on the vessel wall, which can affect blood hemodynamics

significantly(Kallekar, Viswanath, & Anand, 2017).

Some researchers tried to simulate the interaction between blood flow and vessel wall using CFD analysis (Urquiza, Blanco, Vénere, & Feijóo, 2006), (Selmi, Belmabrouk, & Bajahzar, 2019). Abdul Khader, S.M., et al investigated the effect of blood pressure on partially blocked carotid artery wall deformation using a fluidstructure interaction (FSI) model. Their analysis revealed a higher blood pressure caused a larger deformation on the artery wall (Abdul Khader, Ayachit, Pai, Rao, & Kamath, 2012). In a recent study Luo, K., et al. investigated the effect of artery wall stiffness on wall shear stress and found a non-negligible difference in the result between rigid and flexible models (Luo et al., 2019). However, the effect of changes in vascular stiffness on hemodynamics, especially in the micro-sized arteries, has not yet been studied. To overcome such a gap in the literature, in this study the effect of micro-sized arteries elasticity changes on blood pressure, WSS and as well as exerted stress on the capillary wall was investigated using an FSI model.

2. Material and Methods

2.1 Microvessel Models

In this study, the microvessels lumen (L) diameter was selected as 100, 200 and 300 µm. The three models denoted as MV-100, MV-200 and MV-300 (Table 1). The media/lumen rate was selected as 1/10 for all the models (Boari et al., 2008). To obtain more realistic velocity profile the length of models (S) was selected twenty times of lumens diameter (Wood, 1999) (Fig. 1).

Figure 1. Micro-vessels three-dimensional model and geometrical parameters.

Table 1. The microvessels and those geometrical dimensions.

Microvessel	$L(\mu m)$	M	$S(\mu m)$
model		(µm)	
$MV-100$	100	10	2000
$MV-200$	200	20	4000
MV-300	300	30	6000

2.2 Material Properties And Boundary Conditions

Blood flow was modelled as a non-Newtonian fluid using Carreau viscosity properties (Table 2). Also, blood was considered as incompressible fluid with a density of 1060 kg/m^3 (Chong et al., 2017).

Table 2. Viscosity parameters of blood Carreau model (Shibeshi & Collins, 2005)

Blood flow within microvessels was modelled as a pulsatile flow using Fraser et al waveform

(Fraser, Meagher, Blake, Easson, & Hoskins, 2008), (Chong et al., 2017) using User Defined Function (UDF) in ANSYS Fluent (Figures 2 and 3).

A no-slip wall boundary condition was applied to the blood and microvessel contact region in CFD analysis (Siogkas et al., 2015). The CFD analysis of the blood flow was solved using Navier –Stokes equations (Soltani & Chen, 2013).

Figure 2. Time dependent blood flow.

Figure 3. Blood flow direction, coupling domains and FSI region.

For simplification and avoid more complicated finite element analysis the microvessels were assumed to be linearly isotropic materials (Amiri et al., 2019), (Valencia, Ledermann, Rivera, Bravo, &

Galvez, 2008). To determine the effect of lumen stiffness on the blood hemodynamics within them three levels of elasticity $(0.4, 0.6)$ and 0.8 MPa) (Ebrahimi, 2009) were assigned to their material properties.

2.3. Solution and Convergence

Due to the nature of the pulsating flow of blood, both CFD (blood flow) and structural (vessel deformation) analysis were performed transiently. The blood and microvessel domains were meshed using tetrahedral and hexagonal elements respectively (Gómez, Vlad, López, & Fernández, 2016) (Figure 4). The mesh dynamically was updated for the fluid domain at any sub-step, of pulsation of blood flow. Result convergence analysis in CFD calculation was performed using a residual criteria value of 1e-5.

Figure 4. Mesh graphic of fluid (blood) and microvessel domains

3. Results

As shown in Figure 2, the peak velocity of blood flow was seen at around 0.08 seconds of pulsation period, so, the maximum blood pressure (systolic) and WSS were expected to occur at this point. Therefore, in this study, the blood pressure and WSS, as well as the deformation and von-Mises stress in the microvessel wall, were calculated at this time of pulsation.

3.1. Blood Flow

To probe blood flow modality the velocity contour within the micro-vessel was demonstrated in figure 5. As can be seen at the very close distance from the inlet area, the blood flow was fully developed, therefore, we can rely on the CFD analysis result. Moreover, Reynolds numbers were calculated as 2.57, 5.14 and 7.72 for the MV-100, MV-200 and MV-300 models respectively. Such low Reynolds numbers ensured us that blood flow is laminar in CFD analysis.

Figure 5. Blood flow velocity contour in MV-100 model.

The blood velocity contour also shows a decrease in the speed of blood flow from the center to the wall. This phenomenon arises from the no-slip wall boundary condition in the microvessel wall.

3.2. Blood Pressure and WSS

To understand the effect of elasticity change on blood pressure and WSS only maximum magnitude of these quantities was plotted in figure 6. Then the obtained values were normalized by dividing to the result for models with the lowest Young modulus (0.4 MPa). The Maximum pressure for MV-100, MV-200 and MV-300 for the models with the lowest elasticity were 12.2, 11.6 and 10.4 KPa respectively. Similarly, the maximum WSS for the aforementioned models were 1088, 805 and 751 Pa, respectively.

Figure 6. a) Normalized blood pressure and; **b)** WSS for all the models.

Figure 6 shows that with increasing stiffness of the microvessel walls, both blood pressure and WSS increased in all the three models. This increase is more pronounced in MV-100 model than in the other two groups.

3.3. Deformation and von-Mises Stress

To observe the blood flow effect on the microvessel body, the calculated diameter deformation and von-Mises stress for each model were presented (Figure 7).

Figure 7. a) Diameter deformation and; **b)** von-Mises stress in the microvessels.

For all models, the deformation decreased with increasing stiffness so that the deformation of models with the elastic modulus of 0.8 MPa is almost half of that is for models with 0.4 MPa elasticity. In terms of von-Mises stress, there is no significant difference between models with the same size and different stiffness. However, von-Mises stress in models with smaller diameter was higher than models with a bigger diameter. The von-Mises small changes with elasticity changes in microvessels wall showed this parameter change needs a significant variation in microvessels' elasticity.

4. Discussion

As discussed in the introduction section the cardiovascular diseases are very diverse with different origins. In this work, the effect of changes in vascular stiffness in blood pressure and WSS was investigated numerically. While vasodilation is known as the most important way to control hypertension (Giles, Sander, Nossaman, & Kadowitz, 2012), its side effects are always controversial (Nilsson et al., 2020), (Okada et al., 2020). Therefore, finding the causes and roots of hypertension and its symptoms can be an effective step in determining the treatment strategy. The result of this theoretical study shows any change in vascular stiffness can affect blood pressure. As shown in Fig 6.b, for example, doubling the stiffness of a microvessel increased the pressure on it by

about 12%. This phenomenon can also be generalized to WSS. But what highlights the results of this study is the effect of microvessel stiffness on its rate of deformation. Because a possible correlation between blood vessels deformity and atherosclerosis or stroke were showed (Tsai et al., 2013), (Yang et al., 2014). For example, as shown in Figure 7. a, as the stiffness of the microvessel doubles, its deformation is reduced to half. In experimental studies of vascular disease, this reduction in deformation can be considered as a sign of hardening of the vessel. Therefore, the results of this study are a small step in identifying the causes of hypertension and vascular disease.

5. Conclusion

The outcomes of this study can be listed as below:

- I- Microvessels stiffness change affects blood pressure and WSS.
- II- Microvessels deformation in systolic time can significantly decrease with an increase in its stiffness.
- III- The stress in a microvessel structure that arises from blood flow is affected minimally by the microvessels' stiffness.
- IV- The result showed once again that an FSI analysis can be used

as a powerful tool in CVDs studies.

V- Here, the effect of only one parameter on blood pressure was investigated, and a full understanding of the factors influencing hypertension requires more experimental and theoretical studies.

References

Abdul Khader, S. M., Ayachit, A., Pai, B. R., Rao, V. R. K., & Kamath, S. G. (2012). FSI Simulation of Common Carotid under Normal and High Blood Pressures. Advances in Mechanical Engineering, 4, 140579. doi:10.1155/2012/140579

Ali, D., & Önel, S. (2018). Effect of Blood Viscosity on Pressure and Shear Stress on the Walls of an Artery with Stenosis. Paper presented at the 2018 Medical Technologies National Congress (TIPTEKNO).

Amiri, M. H., Keshavarzi, A., Karimipour, A., Bahiraei, M., Goodarzi, M., & Esfahani, J. A. (2019). A 3-D numerical simulation of non-Newtonian blood flow through femoral artery bifurcation with a moderate arteriosclerosis: investigating Newtonian/non-Newtonian flow and its effects on elastic vessel walls. Heat and Mass Transfer, 55(7), 2037-2047. doi:10.1007/s00231-019-02583-4

Boari, G. E., Rizzardi, N., de Ciuceis, C., Platto, C., Paiardi, S., Porteri, E., . . . Rosei, E. A. (2008). Determinants of the structure of resistance-sized arteries in hypertensive patients. Blood Press, 17(4), 204-211. doi:10.1080/08037050802433735

Borén, J., Chapman, M. J., Krauss, R. M., Packard, C. J., Bentzon, J. F., Binder, C. J., . . . Ginsberg, H. N. (2020). Low-density lipoproteins cause atherosclerotic cardiovascular disease: pathophysiological, genetic, and

therapeutic insights: a consensus statement from the European Atherosclerosis Society Consensus Panel. European Heart Journal, 41(24), 2313-2330.

doi:10.1093/eurheartj/ehz962

Casas, R., Castro-Barquero, S., Estruch, R., & Sacanella, E. (2018). Nutrition and Cardiovascular Health. International journal of molecular sciences, 19(12), 3988. doi:10.3390/ijms19123988

Chong, A. Y., Doyle, B. J., Jansen, S., Ponosh, S., Cisonni, J., & Sun, Z. (2017). Blood flow velocity prediction in aorto-iliac stent grafts using computational fluid dynamics and Taguchi method. Computers in Biology and Medicine, 84, 235-246. doi:https://doi.org/10.1016/j.compbiom ed.2017.03.015

Dash, D. (2013). Stenting of left main coronary artery stenosis: A to Z. Heart Asia, $5(1)$, $18-27$. doi:10.1136/heartasia-2012-010218

de Simone, G., Devereux, R. B., Chinali, M., Best, L. G., Lee, E. T., Welty, T. K., & Stong Heart Study, I. (2005). Association of blood pressure with blood viscosity in American Indians - The Strong Heart Study. Hypertension, 45(4), 625-630. doi:10.1161/01.HYP.0000157526.0797 7.ec

Ebrahimi, A. P. (2009). Mechanical properties of normal and diseased cerebrovascular system. Journal of vascular and interventional neurology, 2(2), 155-162.

Flora, G. D., & Nayak, M. K. (2019). A Brief Review of Cardiovascular Diseases, Associated Risk Factors and Current Treatment Regimes. Curr Pharm Des, 25(38), 4063-4084. doi:10.2174/138161282566619092516 3827

Franklin, S. S., & Wong, N. D. (2013). Hypertension and Cardiovascular Disease: Contributions of the Framingham Heart Study. Global Heart, 8(1), 49-57. doi:https://doi.org/10.1016/j.gheart.201 2.12.004

Fraser, K. H., Meagher, S., Blake, J. R., Easson, W. J., & Hoskins, P. R. (2008). Characterization of an Abdominal Aortic Velocity Waveform in Patients with Abdominal Aortic Aneurysm. Ultrasound in Medicine & Biology, 34(1), 73-80. doi:https://doi.org/10.1016/j.ultrasmed bio.2007.06.015

Fuchs, F. D., & Whelton, P. K. (2020). High Blood Pressure and Cardiovascular Disease. Hypertension, 75(2), 285-292. doi:doi:10.1161/HYPERTENSIONAH A.119.14240

Giles, T. D., Sander, G. E., Nossaman, B. D., & Kadowitz, P. J. (2012). Impaired Vasodilation in the Pathogenesis of Hypertension: Focus on Nitric Oxide, Endothelial-Derived Hyperpolarizing Factors, and Prostaglandins. The Journal of Clinical Hypertension, 14(4), 198-205. doi:10.1111/j.1751-7176.2012.00606.x

Gómez, S., Vlad, M. D., López, J., & Fernández, E. (2016). Design and properties of 3D scaffolds for bone tissue engineering. Acta Biomaterialia, 42, 341-350. doi:http://dx.doi.org/10.1016/j.actbio.2

016.06.032

Hoi, Y., Woodward, S. H., Kim, M., Taulbee, D. B., & Meng, H. (2006). Validation of CFD simulations of cerebral aneurysms with implication of geometric variations. Journal of Biomechanical Engineering, 128(6), 844-851. doi:10.1115/1.2354209

Kallekar, L., Viswanath, C., & Anand, M. (2017). Effect of Wall Flexibility on the Deformation during Flow in a Stenosed Coronary Artery. Fluids, 2(2). doi:10.3390/fluids2020016

Katt, M. E., Linville, R. M., Mayo, L. N., Xu, Z. S., & Searson, P. C. (2018). Functional brain-specific microvessels from iPSC-derived human brain microvascular endothelial cells: the role of matrix composition on monolayer formation. Fluids and Barriers of the CNS, 15(1), 7. doi:10.1186/s12987-018-0092-7

Lipp, S. N., Niedert, E. E., Cebull, H. L., Diorio, T. C., Ma, J. L., Rothenberger, S. M., . . . Goergen, C. J. (2020). Computational Hemodynamic Modeling of Arterial Aneurysms: A Mini-Review. Frontiers in Physiology, 11, 454-454. doi:10.3389/fphys.2020.00454

Lozano, R., Naghavi, M., Foreman, K., Lim, S., Shibuya, K., Aboyans, V., . . . Memish, Z. A. (2012). Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet, 380(9859), 2095-2128. doi:10.1016/s0140-6736(12)61728-0

Luo, K., Jiang, W., Yu, C., Tian, X., Zhou, Z., & Ding, Y. (2019). Fluid– Solid Interaction Analysis on Iliac Bifurcation Artery: A Numerical Study. International Journal of Computational Methods, 16(07), 1850112.

doi:10.1142/s0219876218501128

Markwald, R. R., Norris, R. A., Moreno-Rodriguez, R., & Levine, R. A. (2010). Developmental basis of adult cardiovascular diseases: valvular heart diseases. Annals of the New York Academy of Sciences, 1188, 177-183. doi:10.1111/j.1749-6632.2009.05098.x

Miller, M. R., & Newby, D. E. (2019). Air pollution and cardiovascular disease: car sick. Cardiovascular

Research, 116(2), 279-294. doi:10.1093/cvr/cvz228

Mittal, R., Seo, J. H., Vedula, V., Choi, Y. J., Liu, H., Huang, H. H., . . . George, R. T. (2016). Computational modeling of cardiac hemodynamics: Current status and future outlook. Journal of Computational Physics, 305, 1065-1082.

doi:https://doi.org/10.1016/j.jcp.2015.1 1.022

Nilsson, K. F., Gozdzik, W., Zielinski, S., Ratajczak, K., Goranson, S. P., Rodziewicz, S., . . . Frostell, C. (2020). Pulmonary Vasodilation by Intravenous Infusion of Organic Mononitrites Of 1,2-Propanediol in Acute Pulmonary Hypertension Induced by Aortic Cross Clamping and Reperfusion: A Comparison With Nitroglycerin in Anesthetized Pigs. Shock, 54(1), 119-127. doi:10.1097/shk.0000000000001436

O'Donnell, M. J., Xavier, D., Liu, L., Zhang, H., Chin, S. L., Rao-Melacini, P., . . . Yusuf, S. (2010). Risk factors for ischaemic and intracerebral haemorrhagic stroke in 22 countries (the INTERSTROKE study): a casecontrol study. Lancet, 376(9735), 112- 123. doi:10.1016/s0140- 6736(10)60834-3

Okada, S., Fukunaga, S., Ohta, H., Furuta, T., Hirano, R., Motonaga, T., & Ishikawa, Y. (2020). Cerebral Insufficiency Caused by Diazoxide in a Premature Neonate with Congenital Hyperinsulinism. Neuropediatrics, 51(03), 211-214. doi:10.1055/s-0039- 3400975

Rapsomaniki, E., Timmis, A., George, J., Pujades-Rodriguez, M., Shah, A. D., Denaxas, S., . . . Hemingway, H. (2014). Blood pressure and incidence of twelve cardiovascular diseases: lifetime risks, healthy life-years lost, and age-specific associations in 1·25

million people. Lancet, 383(9932), 1899-1911. doi:10.1016/S0140- 6736(14)60685-1

Ren, R., Covassin, N., Yang, L., Li, Y., Zhang, Y., Zhou, J., . . . Tang, X. (2018). Objective but Not Subjective Short Sleep Duration Is Associated With Hypertension in Obstructive Sleep Apnea. Hypertension, 72(3), 610-617. doi:10.1161/HYPERTENSIONAHA.1 18.11027

Selmi, M., Belmabrouk, H., & Bajahzar, A. (2019). Numerical Study of the Blood Flow in a Deformable Human Aorta. Applied Sciences-Basel, 9(6), 11. doi:10.3390/app9061216

Shibeshi, S. S., & Collins, W. E. (2005). The Rheology of Blood Flow in a Branched Arterial System. Appl Rheol, 15(6), 398-405. doi:10.1901/jaba.2005.15-398

Siogkas, P. K., Papafaklis, M. I., Sakellarios, A. I., Stefanou, K. A., Bourantas, C. V., Athanasiou, L. S., . . . Fotiadis, D. I. (2015). Patient-specific simulation of coronary artery pressure measurements: an in vivo threedimensional validation study in humans. Biomed Research International, 2015, 628416-628416. doi:10.1155/2015/628416

Soltani, M., & Chen, P. (2013). Numerical Modeling of Interstitial Fluid Flow Coupled with Blood Flow through a Remodeled Solid Tumor Microvascular Network. Plos One, 8(6), e67025. doi:10.1371/journal.pone.0067025

Tsai, W. C., Sun, Y. T., Liu, Y. W., Ho, C. S., Chen, J. Y., Wang, M. C., & Tsai, L. M. (2013). Usefulness of Vascular Wall Deformation for Assessment of Carotid Arterial Stiffness and Association With Previous Stroke in Elderly. American

Journal of Hypertension, 26(6), 770- 777. doi:10.1093/ajh/hpt027

Urquiza, S. A., Blanco, P. J., Vénere, M. J., & Feijóo, R. A. (2006). Multidimensional modelling for the carotid artery blood flow. Computer Methods in Applied Mechanics and Engineering, 195(33), 4002-4017. doi:https://doi.org/10.1016/j.cma.2005. 07.014

Valencia, A., Ledermann, D., Rivera, R., Bravo, E., & Galvez, M. (2008). Blood flow dynamics and fluidstructure interaction in patient-specific bifurcating cerebral aneurysms. International Journal for Numerical Methods in Fluids, 58(10), 1081-1100. doi:10.1002/fld.1786

Vardhan, M., Gounley, J., Chen, S. J., Kahn, A. M., Leopold, J. A., & Randles, A. (2019). The importance of side branches in modeling 3D hemodynamics from angiograms for patients with coronary artery disease. Scientific Reports, 9(1), 8854. doi:10.1038/s41598-019-45342-5

Wang, Y. F., Quaini, A., & Canic, S. (2018). A Higher-Order Discontinuous Galerkin/Arbitrary Lagrangian Eulerian Partitioned Approach to Solving Fluid-Structure Interaction Problems with Incompressible, Viscous Fluids and Elastic Structures. Journal of Scientific Computing, 76(1), 481- 520. doi:10.1007/s10915-017-0629-y

Wood, N. B. (1999). Aspects of Fluid Dynamics Applied to the Larger Arteries. Journal of Theoretical Biology, 199(2), 137-161. doi:https://doi.org/10.1006/jtbi.1999.09 53

Wu, C.-Y., Hu, H.-Y., Chou, Y.-J., Huang, N., Chou, Y.-C., & Li, C.-P. (2015). High Blood Pressure and All-Cause and Cardiovascular Disease Mortalities in Community-Dwelling Older Adults. Medicine, 94(47), e2160e2160.

doi:10.1097/MD.0000000000002160

Yamagishi, K., Sawachi, S., Tamakoshi, A., Iso, H., & Group, f. t. J. S. (2019). Blood pressure levels and risk of cardiovascular disease mortality among Japanese men and women: the Japan Collaborative Cohort Study for Evaluation of Cancer Risk (JACC Study). Journal of Hypertension, 37(7), 1366-1371.

doi:10.1097/hjh.0000000000002073

Yang, J. W., Cho, K. I., Kim, J. H., Kim, S. Y., Kim, C. S., You, G. I., . . . Lee, J. W. (2014). Wall shear stress in hypertensive patients is associated with carotid vascular deformation assessed by speckle tracking strain imaging. Clinical hypertension, 20, 10-10. doi:10.1186/2056-5909-20-10

Yoganathan, A. P., Cape, E. G., Sung, H. W., Williams, F. P., & Jimoh, A. (1988). Review of hydrodynamic principles for the cardiologist: applications to the study of blood flow and jets by imaging techniques. J Am Coll Cardiol, 12(5), 1344-1353. doi:10.1016/0735-1097(88)92620-4

Zhang, J. M., Zhong, L., Su, B., Wan, M., Yap, J. S., Tham, J. P., . . . Tan, R. S. (2014). Perspective on CFD studies of coronary artery disease lesions and hemodynamics: a review. Int J Numer Method Biomed Eng, 30(6), 659-680. doi:10.1002/cnm.2625