The Study of Hemodynamics Phenomena in Intracranial Aneurysms with Computational Fluid Dynamics (CFD): A PRISMA - Compliant Systematic Review

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Abstract: ***Aneurysms are pathological dilatations of some parts of the human vascular system and are characterized by thin and dilated regions in the arterial wall. The most common aneurysm is the intracranial aneurysms (IAs) which consist of dilatations of cerebral arteries circle. The causes of IAs have been investigated so long and so hard over the years and the majority of researchers agree that hemodynamic phenomena like blood flow play an important role in the formation, growing, and rupture of a brain aneurysm. However, proposed experiments, with the aim of a better understanding of the characteristics of blood flow in aneurysms, are still difficult to take. OBJECTIVE: The objective of this study was to review the literature on the overall clinical importance of blood flow in IAs and to compare early categories of numerical analysis of blood flow. METHODS: The author performed a systematic electronic search in the PubMed database over the last 5 years using the terms "Numerical analysis of blood flow and hemodynamic phenomena". RESULTS: 450 full-text manuscripts were retrieved and 437 were excluded due to inclusion criteria. The Computacional Fluid Dynamics (CFD) approach was used in overall studies to perform numerical simulations with vascular wall models and numerical modeling of cerebral arteries, to describe the blood flows of the models of giant cerebral aneurysm before and after flow diverter implantation at the aneurysmal sac and to evaluate flow modification effects introduced by endovascular therapy in real treatment cases. Changes in blood flow, before and after stent deployment, are presented in some studies. For instance, Wall Shear Stress (WSS) on the aneurysmal sac dropped from 0.69 Pa to 0.48 Pa after the flow diverter implantation; CONCLUSION: The CFD methods can be effectively used to evaluate changes in blood flow before and after diverter implantation, describe the behavior of the cerebral vascular walls in a realistic fashion.***

Keywords: Computacional Fluid Dynamics, blood flow, Intracranial aneurysm, hemodynamic phenomena, Numerical analysis

1. Introduction

Aneurysms are pathological dilatations of some parts of the human vascular system and are characterized by thin and dilated regions in the arterial wall. The most common aneurysm is the intracranial aneurysms (IA) which consist of dilatations of cerebral arteries circle. According to Linkai Jing et al [1], aneurysms are present in 2%–5% of the general population and the annual risk of rupture is 0.7%–1.9% causing subarachnoid hemorrhage (SAH) [1] with consequent death or permanent sequelae in the patient. The causes of intracranial aneurysms have been investigated so extensive over the years and the majority of researchers agree that hemodynamic phenomena play a fundamental role in aneurismal formation, growing, and rupture [2][3]. However, proposed experiments, with the aim of a better understanding of the characteristics of blood flow (BF) in the aneurysm, are still difficult to take. Nevertheless, with the development of modeling techniques of cerebral vascular systems, computational fluid dynamics (CFD) has become a popular tool for studying such hemodynamics phenomena and better understanding geometric aspects of aneurysms [3-7]. Hence, in this paper, a literature search was performed to address CFD, their efficacy, safety, limitations, developments and their way to report associated hemodynamic phenomena. This article was organized and established as a systematic review [8].

2. Methods

To conduct a literature review, a systematic electronic search was performed using the PubMed database on all available articles published from January 2015 to February 2020. The terms "Brain aneurysm: formation, growing, and rupture"; "Brain aneurysm: numerical analysis of blood flow" and "Numerical analysis of blood flow and the association with hemodynamic phenomena" were used to retrieve and analyze abstracts, full-text manuscripts where CFD was involved or fully addressed in blood flow domain and the reference lists from PubMed database. Case reports, reviews studies and preliminary results were excluded. The resulting flow chart is shown in Figure 1.

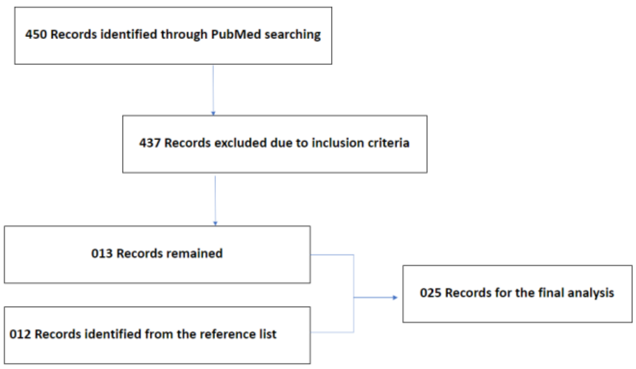

Figure 1: Flow chart of the search strategy

3. Results and Discussion

After a review of the retrieved literature, the current status of CFD methods in IA was summarized in terms of numerical simulation involved in predictions of surgical operations and behavior of the cerebral arteries; virtual deployment of flow diverters in models of giant IA; the assessment of changes in BF before diverter implantation; the dependence of BF reconstruction of graphical resolution and special complexity and measuring changes in flow velocity; wall shear stress (WSS) before and after stent implantation.

I - Numerical simulation involved in predictions of surgical operations and behavior of the cerebral arteries

I.1 - Aneurysm therapy basis

According to Ivanov [9], many researchers, e.g. [10-14], agree that mechanical factors such as hemodynamic forces, blood pressure and WSS are relevant information for understanding the processes of aneurysm initiation, growth and rupture. Yet, as started by [9], [10], WSS is the most suitable mechanical factor used to describe the process of aneurysm formation and behaviors. Nevertheless, in modern medical diagnostic methods, WSS is not fitted enough to predict surgical operations and decide for an acceptable cerebral aneurysm therapy [9]. Today, the basis of aneurysm therapies includes not only mechanical factor like WSS but also patient history, aneurysm size and location [9].

I.2 - Studies performed with CFD methods

In study conducted in [9], CFD and, in particular, fluid-structure interaction simulations (FSIS) were used to develop biomechanical and numerical models of healthy and pathological cerebral arteries. The developed models were used to study and access meaningfully information to clinicians not only understanding of the processes of the aneurysm initiation, growth and rupture but also propose the best therapy for patients.

Initially, the study was dedicated to the vessel wall model selection. Three types of vessel wall models were addressed: rigid, perfectly elastic and hyperelastic. Next, the study considered two patient-specific aneurysms of the left posterior cerebral arteries (PCA) taking into consideration patient-specific boundary conditions at the inlet [9].

I.3 - Results of vessel wall model selection

The simulations with the three arterial wall models produced the following results: in the case of rigid vessel walls the BF for healthy left PCA and left PCA with aneurysm do not differ during cardiac cycle [9]; blood flow for left PCA with stenosis decreased by 10% on average [9]. In the case of perfectly elastic walls, similar situation was observed [9]. As for the case of hyperelastic walls model, the BF behavior was different from rigid and elastic walls. Left PCA in healthy state showed the highest BF [9]. BF through the left PCA with aneurysm decreased by 6% compared with normal artery and BF through the stenosed left PCA decreased by 11% compared with healthy artery [9]. Therefore, as far as comparative analysis as concern, hyperelastic wall model shown the most adequate and realistic result [9].

I.4 - Results of patient-specific numerical investigation

The mentioned study also presents results of the patient-specific numerical investigation of basilar artery and PCA in healthy state, with stenosis and aneurysms of different sizes, as can be seen on figure 1.

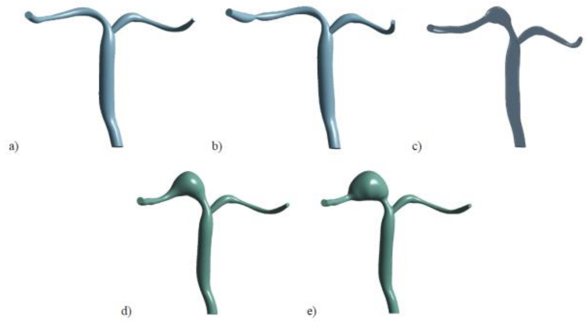

Figure 2: Basilar artery with PCA: (a) normal state, (b) stenosis, (c), (d) and (e) aneurysm with different sizes [9]

In the study of patient-specific aneurysms of the left PCA two models of the left PCA with small and large aneurysms were investigated by the authors of the paper [9]. The investigated models are showed in figure 1d-1e.

The result of the investigations of BFs at the outlets of the left PCA for both of the models indicated that increasing the size of the aneurysm ends up to reduce the BF at the outlet of the affected artery [9]. The difference in blood flow rates for the models was around 17% [9].

As for the investigations of BFs at the outlets of the right healthy PCA for both aneurysm models, the results shown that the decrease in BF through the pathological left PCA and the associated growth of the aneurysm leads to an increase of BF through the healthy branch [9].

The WSS for the two investigated models at systole and diastole condition in the dome of the aneurysms was low due to reduced blood velocity at the inlet and reduced blood flow through the dome [9].

I.5 - Conclusion

In conclusion, the paper [9] point out the computational and biomechanics relevancy of CFD on the discussion of the mechanical factor that influence the formation, growth and rupture of cerebral aneurysms. Hyperelastic wall model and interaction between blood and wall meaningfully change hemodynamics of the aneurysm rather than rigid wall model. Patient-specific modeling needs not only the geometry of the individual patient but also the individual boundary conditions. In addition, the geometry of an aneurysm plays an important role on hemodynamics and stress-strain state of the aneurysm wall.

II - Virtual deployment of flow diverters in models of giant IA

Flow diverter is a modified stent device with higher metal coverage rate than the usual stent and it is deployed endovascularly to treat giant cerebral aneurysms (GCA) [6]. In the study addressed in [6] the model of a GCA was selected to be treated by the virtual flow diverter implantation technique. The BFs behaviors in the aneurysm before and after the treatment were simulated numerically by CFD method. Such a simulation provided a numerical investigation of the most common hemodynamics factors related to the regrowth and rupture, that is, velocity, flow rate, WSS among others.

II.1 - Basis of virtual deployment of flow diverters in GCA

The basis of GCA modeling was patient-specific model of cerebral aneurysm, virtual implantation of the flow diverter, mesh generation and boundary conditions [6].

Patient-specific model of cerebral aneurysm

Figure 2 shows the patient-specific reconstructed 3D model of the giant aneurysm used in the virtual treatment before and after a flow diverter deployment [6]. In the aneurysm model, the diameter of the inlet, outlet and small branch are 4.4 mm, 3.8 mm and 1.8 mm, respectively. The maximum diameter of the giant aneurysm is 25 mm and the aspect ratio (Depth/Width) is about 0.82 [6].

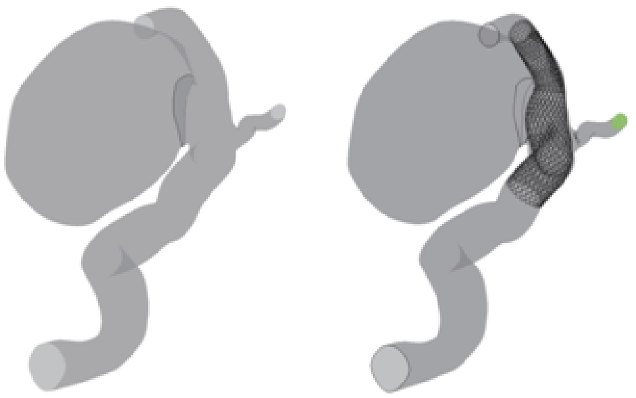

Figure 3: A giant cerebral aneurysm before and after the virtual deployment of a flow diverter [6]

Virtual implantation of the flow diverter

In the study performed in [6] the giant cerebral aneurysm was treated virtually by a flow diverter implantation. The flow diverter deployment is entirely described in mentioned study. In Figure 2, the model of the giant aneurysm with the flow diverter implantation (mesh portion) is shown on the right.

Mesh generation

As print out in [6], the computational meshes of the aneurysm models were generated by Ansys ICEM-CFD 13.0. The numbers of elements in the computational meshes generated for the aneurysm model before the flow diverter implantation were 1,282,6627 (number of nodes), 611,281 (number of elements). The total number of meshes computational elements after the flow diverter implantation was 2,164,973 (number of nodes) and 12,012,340 (number of elements) [6].

Boundary conditions

In the study conducted in [6], the following boundary condition was assumed in the virtual treatment of GCA: The artery wall was assumed to be rigid; a parabolic velocity profile was imposed at the inlet; the average velocity at the inlet was calculated in a specific fashion to guarantee the average WSS at the inlet artery to be 1.5 Pa; a reference pressure of 10000 Pa was adopted at the outlets.

II.2 - Results and discussion

The achieved results in the study were presented in terms of the BF behaviors, distribution of pressure, velocity and WSS on the aneurysmal sac before and after the flow diverter implantation [6].

The results of BF behaviors, measured from streamline and flow pattern, shown that the velocity decreased remarkably and the flow structure became simpler after the flow diverter implantation. The distribution of velocity inside the aneurysmal sac shown a remarkably velocity reduction after the flow diverter implantation. The average velocity inside the aneurysmal sac decreased from 0.057 m/s to 0.023 m/s [6]. The pressure on the aneurysmal sac increased from 10646 Pa to 11723Pa as a consequence of resistance increased after the flow diverter implantation [6]. As for the distribution of WSS, the results shown that the average WSS on the aneurysmal sac decreased from 0.69 Pa to 0.48 Pa after the flow diverter implantation but the WSS located at the distal side of the aneurysmal neck increased to 22 Pa from 15 Pa at the same circumstance [6].

II.3 - Conclusion

The author of paper [6] concluded that the flow pattern is simplified and the velocity inside the aneurysmal sac is reduced remarkably after the flow diverter implantation. The averaged WSS on the aneurysmal sac is decreased from 0.69 Pa to 0.48 Pa, thus the regrowth risk of the aneurysm will be reduced after flow diverter implantation.

III - The assessment of changes in BF before diverter implantation

III.1 - Study performed

The paper [13] benchmarks two representative CFD solvers in simulating blood flow in a patient-specific IA model, that is: ANSYS Fluent, a commercial finite volume (FV)-based solver and VMTKLab multidGetto, a discontinuous Galerkin (dG) finite element (FE)-based solver [13].

III.2 - Results and discussions

The accuracy of ANSYS Fluent improved by increasing the spatial mesh resolution (134k, 1.1m, 8.6m and 68.5m tetrahedral element meshes) [13]. The VMTKLab accuracy increased by increasing the degree of polynomials (first, second, third and fourth degree) on the base 134k tetrahedral element mesh [13].

The results show that high-order VMTKLab provide better accuracy per degree of freedom but worse accuracy per Jacobian non-zero entry as compared to ANSYS Fluent. Both CFD solvers converged to the same numerical solution but there was a discrepancy between under-resolved velocity fields suggesting that mesh independence was reached following different paths [13].

III.3- Conclusion

The results obtained in [13] clearly show that CFD methods can be used to evaluate changes in BF before diverter implantation and describe the behavior of the cerebral vascular walls in realistic fashion.

IV - The dependence of BF reconstruction of graphical resolution and special complexity

IV.1 – The basis of Study

As addressed in, e.g. [10 – 13], [14 – 25], computational simulations of BF have been used to assist clinical decisions in evaluating the risk of rupture of an aneurysm. CFD methods allows the computation of blood pressure and WSS which are considered important factors in vascular diseases [10 – 13]. The accuracy of CFD methods depend heavily on the underlying model assumptions, the model parameters [17, 18], the boundary conditions [19, 20], and the segmentation of the vascular geometry [14]. These parameters are specific to each patient [19, 21] and partially or fully unknown [14]. Yet as opposed to physical measurement techniques, CFD allows for nearly arbitrary high resolution [14].

Nun-invasive measurement techniques, such as ultrasound or phase-contrastmagnetic resonance imaging (PC-MRI) are responsible for the low resolution in patient-specific data [14]. While PC-MRI provides 4D (3D space and time) images of velocity at a spatial resolution between 0.3-0.7 mm the normal resolution observed in CFD is 0.1-0.2 mm, e.g. [14], [15, 22].

To deal with the discrepancy between CFD simulations and PC-MRI measurements [14, 22, 23], data assimilating techniques, in particular variational data assimilation e.g. [24, 25], a combination of CFD and 4D MRI, has been currently applied to blood flow models [14]. This technique can identify unknown model parameters such that the difference between physical observations and model results are minimized [14].

The aim of the study presented in [14] was to derive and implement variational data assimilation for transient hemodynamics, investigating its feasibility and robustness on cerebral aneurysms with coarse and noisy velocity measurements.

IV.2 - The development of variational data assimilation

In the studies performed in [14], the variational data assimilation approach was performed on two numerical simulation. The first one considered an idealized 3D aneurysm-like (2D space and time). The second one reconstructed the flow conditions in a real aneurysm from a 4D MRI scan.

2D Aneurysm

Figure 3 shows a 2D blood vessel bifurcation model with an aneurysm. This model was used to test the robustness of the assimilated solution against incomplete observations, noisy observations and regularization parameters. In addition, the 2D model was used to compare the quality of the reconstruction for two types of observation operators [14].

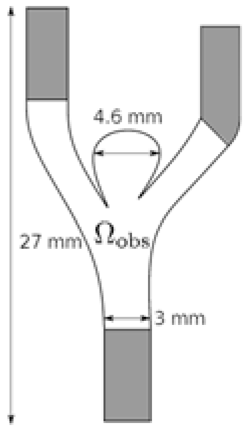

Figure 3: The computational domain for the 2D aneurysm experiment. The grey area is used to generate the physical observations [14]

Flow reconstruction in an aneurysm from 4D MR

The variational data assimilation approach was tested on real measurements of a dog's blood vessel with an artificially introduced aneurysm. The physical measurements were obtained using 4D PC-MRI [14].

VI.2 - Results and discussion

The results print out in [14], concerned to numerical experiments of a synthetic 3D aneurysm model (time and 2D space) case, indicate that the variational data assimilation is robust with respect to pointwise Gaussian measurement noise and to the regularization parameters. The results also shown the reconstruction becomes worse if the number of measurements is decreased and the technique is feasible for 4D (time and 3D space) problems as well.

VI.3 - Conclusion

The author concluded that variational data assimilation, a combination of CFD and 4D MRI, applied in blood flow models with suitable regularization, accurately reconstructs flow, even in the presence of significant noise.

4. Conclusion

Many researchers, e.g. [10-18], agree that mechanical factors such as hemodynamic forces, blood pressure and WSS are relevant information for understanding the processes of aneurysm initiation, growth and rupture. The overall studies presented in this paper review shown that the assessment of detailed hemodynamic properties using image-based simulations via CFD methods can provide helpful information about the aneurysm behavior. Nevertheless, the clinical applicability of these methods has been limited so far.

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Some studies addressed here, particularly those which compare their simulation results to other research centers, demonstrated that there exists a considerable difference between their final simulation results. Specific analysis of the individual procedures revealed some weaknesses of CFD approaches in image preprocessing/postprocessing domain. Hence, there is a need to establish a standard metric to measure the quality of the model performed in terms of robustness of the simulation results. Considering such metric, it is important to raise the awareness of the sources of weaknesses, limitation and uncertainty of CFD methods.

Regarding the use of CFD methods to develop hemodynamic models to predict surgical operations and decide on acceptable brain aneurysm therapy [6] the following limitations were identified: (1) The arterial wall is anisotropic and contains three layers but the homogeneous and isotropic wall model used in computational simulations may lead, in some circumstance, to inaccurate predictions of the wall deformation field and hemodynamic solution; (2) CFDs methods are limited to model some vessel wall properties from tomographic images [6]. For instance, the wall thickness is practically impossible to obtain from tomograms. In studies conducted in [6] an average morphological data for wall thickness parameter was used. Hence, for a more precise description of the WSS and hemodynamics the authors of the paper point out that the morphological data for the wall thickness for each particular patient on the basis of medical diagnostic data is necessary.

As for the modeling of hemodynamics in intracranial aneurysms, the CFD methods revel uncertainties that might dominate over the spatial and temporal errors of the numerical solution, namely: (1) The uncertainty in the computational domain representation; (2) The uncertainty in boundary conditions imposed on fictitious inflow and outflow boundaries; (3) The assumption of rigid walls or the uncertainty in actual response of the wall in fluid-structure interaction computations. (4) The uncertainty in the constitutive law for blood, in particular for low-speed flows or high-speed flows with transition to turbulence [13]. All in all, to give precise meaning to accuracy requirements, the author of the paper [13] point out that the precision should be related to uncertainty in the inputs to the mathematical model by means of sensitivity analysis. Moreover, people tend to work in interdisciplinary fashion in order to model hemodynamics in IA. Precisely, physicians, medical imaging experts, bio-medical engineer and computer sciences researchers collaborate using a common language for the overall tasks. As domain experts go outside their actual expertise, user-induced errors or uncertainty are likely to happen.

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