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Impact of patient-specific inflow boundary conditions on intracranial aneurysm hemodynamics

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Abstract: For hemodynamic simulations of intracranial aneurysms boundary conditions (BC) are required. In most cases, these are not patient-specific and thus do not reflect the real flow conditions in the patient. This study investigates the influence of patient-specific inflow BC on intra-aneurysmal hemodynamics. The focus lies on gender and age variations of the patients. To asses the impact, four different inflow curves representing the velocity profile of the inflow over one cardiac cycle is modeled. These four inflow BC are varied in the simulations of each aneurysm from selected subgroups. From the results of the simulations, the hemodynamic parameters are determined for each inflow BC and the percent differences between inflow BC are determined. The results show that the hemodynamic parameters are not robust to varying inflow BC. It can be seen that age has more influence on the hemodynamic parameters than gender. This study demonstrates the dependence of valid hemodynamic parameters on realistic inflow BC. Thus, if available, patient-specific inflow curves are recommended.

Keywords: intracranial aneurysms, computational fluid dynamics, hemodynamics, boundary conditions

1 Introduction

An intracranial aneurysm is a local, pathological vascular dilatation of the cerebral arteries. Due to the high prevalence of 3% [9] of intracranial aneurysms and the risk of rupture with a possible subarachnoid hemorrhage, it is of medical interest to identify the individual rupture risks. Computer-aided simulations of intra-aneurysmal blood flow are a useful tool for the individual risk analysis, since direct blood flow measurement is not possible. This allows approximation of hemodynamic parameters that might correlate with potential rupture risk [1]. For computer-aided simulations, it is necessary to create patient-specific models from medical image data. These serve as a basis for the blood flow simulations within the vessels. In addition, it is necessary to define several BC for the simulation. In contrast to the models, these BC are usually not patient-specific, since the values can often only be measured in vivo with high effort and are thus not always available. Therefore, generalizations of the actual condition are made and measurements or values from the literature are used. This leads to the fact that the calculated hemodynamic parameters deviate from the real values. Existing studies already show the influence of varying BC on blood flow and thus on rupture risk analysis [7, 10]. This study investigates the effect of inflow BC on intra-aneurysmal hemodynamics. For this purpose, four representative inflow curves are generated, which reflect the patient-specific characteristics regarding age and gender, are applied to eight patient-specific aneurysm models from a respective subgroup. Consequently, for each aneurysm four simulations are performed with the varying inflow BC, where one inflow BC corresponds to the patient's age and gender and is thus considered as patient-specific. With the help of the simulations, the hemodynamic parameters can be determined and the influence of the characteristics age and gender can be investigated.

2 Material and Methods

2.1 Patient Selection

For patient selection, subgroups were defined, which show differences only in one specific characteristic. All eight cases are bifurcation aneurysms of the anterior communicating artery (Acom) without multiple aneurysms. Table 1 shows the categorization of the subgroups, whereby Case 1 (over 60 years), Case 2 (between 40 and 60 years) and Case 3 (under 40 years) divided the patients into age groups for which both genders were selected.

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Tab. 1: Selected cases and the patient-specific characteristics of gender, age and rupture status.

Case	Gender	age	rupture status
1.1a	female	65	unruptured
1.1b	male	69	unruptured
1.2a	female	68	ruptured
1.2b	male	68	ruptured
2a	female	51	ruptured
2b	male	50	ruptured
3a	female	35	ruptured
3b	male	36	ruptured

2.2 Inflow Curve Generation

For the creation of the four different inflow curves, two representative curves from Xu et al. [11] were taken which are assigned to the male gender. The curves originate from different age structures, so that they can be assigned to youngMale (under 60 years) and oldMale (over 60 years). With the help of existing studies, gender differences representing variations in systolic and diastolic peaks are extracted [12]. The available curves are modified to youngFemale (under 60 years) and oldFemale (over 60 years) using Matlab (MATLAB Version R2018a; The Mathworks Inc.; Massachusetts; USA) (see Figure 1).

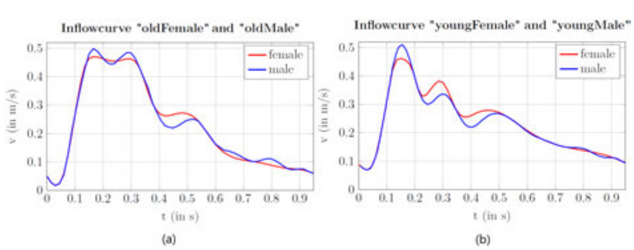

Fig. 1: Inflow curves over one cardiac cycle for the male (a) and female gender (b).

2.3 Hemodynamic Simulation

For the time-dependent blood flow simulations a finite-volume-based computational fluid dynamics (CFD) approach using Star CCM+ 2020.1 (Siemens Product Lifecycle Management Software Inc.; Plato; TX; USA) is applied. For the spatial discretization polyhedral and prism cells with a base size of $0.15\ \mathrm{mm}$ are used for the generation of the volume meshes. Three prism layers with a growth rate of 1.3 are applied to account for the occurring velocity gradients. For the inlet BC the inflow curves depicted in Figure 1 are used. At the outlets constant pressure $p = 0$ is applied and the vessel walls are assumed to be rigid with no-slip conditions. The blood is considered as an incompressible ($\rho = 1055\ \frac{\mathrm{kg}}{\mathrm{m}^3}$), Newtonian ($\eta = 4\ \mathrm{mPa \cdot s}$) fluid with laminar flow conditions. For all patient-specific models, two cardiac cycles are simulated, whereas only the last is included in the calculation of the hemodynamic parameters.

2.4 Analysis

Based on the time-dependent simulations, different hemodynamic parameters are calculated using the 3D post-processing software EnSight 10.2.8 (ANSYS Inc.; Canonsburg; PA; USA):

- **Time-averaged Wall Shear Stress (AWSS)** describes the tangential shear stress along the luminal vessel wall averaged over one cardiac cycle.
- **Oscillatory Shear Index (OSI)** is a metric to describe the change in magnitude and direction of wall shear stress throughout one cardiac cycle.
- **Inflow Concentration Index (ICI)** representing the inflow concentration into the aneurysm related to the parent vessel.

3 Results

In this study hemodynamic parameter deviations are compared qualitatively as well as quantitatively. Considering the exemplary qualitative AWSS representations for Case 3b (see Figure 2), the AWSS appears very similar for all inflow curves. Slight differences can be seen in the inflow curves of the older patients which show a larger area of high AWSS compared to the inflow curves of the young patients (see arrows in Figure 2). A difference of the AWSS between the inflow curves for the genders of one age group is not clearly recognizable.

In order to quantitatively assess the parameter variations, the relative deviation between the suited curve, which matches the patient based on their specific characteristics, and the unsuited curve, having the highest parameter deviation from the suited curve, is determined for each case. This demonstrates which inflow variation has the highest influence on the respective parameter.

Table 2 shows these relative deviations for the AWSS. For the younger patients, the highest deviations occur when using the inflow curves of the older patients. For example, in Case 3a, the patient-specific curve is the youngFemale inflow curve. If this case is simulated with all four inflow curves, the result shows that the inflow curve oldMale differs most considerably from the patient-specific curve. The same relations

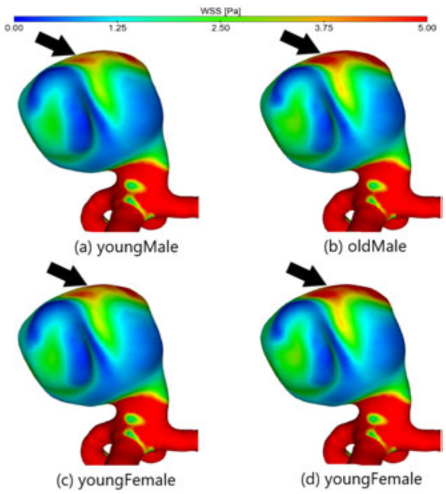

Fig. 2: Representation of the AWSS from Case 3b for the four different inflow curves (a-d). The areas showing differences between the age groups are marked with arrows.

Tab. 2: Relative deviation of AWSS when comparing patient-specific suited curve to unsuited curve. The case with the largest deviation is printed in bold.

Case	suited curve	unsuited curve	relative deviation
1.1a	oldFemale	youngMale	-13.45 %
1.1b	oldMale	youngMale	-10.43 %
1.2a	oldFemale	youngMale	-10.40 %
1.2b	oldMale	youngMale	-9.30 %
2a	youngFemale	oldMale	12.33 %
2b	youngMale	oldMale	17.36 %
3a	youngFemale	oldMale	8.06 %
3b	**youngMale**	**oldFemale**	**17.51 %**

can be observed for the older patients of Case 1.1 and 1.2.
For the impact of the inflow on the ICI, Table 3 indicates that for Case 2 and Case 3 in all four simulations, regardless of gender, the oldFemale inflow curve leads to the largest deviations. For the older patients, an inflow curve of a younger patient leads to the largest deviation in three scenarios. The largest relative deviation is 55.24 % in Case 1.2a between the ICI values of the inflow curve oldFemale and youngMale. For the effect on OSI, it is visible in Table 4 that for Case 1.1 and for Case 1.2, the inflow curve of the other age group leads to the highest difference regarding the OSI. This behavior can be seen for Case 2 and Case 3 with one exception as well. No pattern can be identified for the influence of gender in this table. For example, in Case 1.2, regardless of patient gender, the youngFemale inflow curve produces the largest deviation in average OSI. Case 1.1a shows the largest relative difference (73.09 %) in terms of OSI for the inflow curves oldFemale and youngMale.

Tab. 3: Relative deviation of ICI when comparing patient-specific suited curve to unsuited curve. The case with the largest deviation is printed in bold.

Case	suited curve	unsuited curve	rel. deviation
1.1a	oldFemale	youngFemale	46.11 %
1.1b	oldMale	oldFemale	-3.23 %
1.2a	**oldFemale**	**youngMale**	**55.24 %**
1.2b	oldMale	youngMale	27.57 %
2a	youngFemale	oldFemale	-14.03 %
2b	youngMale	oldFemale	-18.01 %
3a	youngFemale	oldFemale	-13.52 %
3b	youngMale	oldFemale	-31.47 %

Tab. 4: Relative deviation of OSI when comparing patient-specific suited curve to unsuited curve. The case with the largest deviation is printed in bold.

Case	suited curve	unsuited curve	rel. deviation
1.1a	**oldFemale**	**youngMale**	**73.09** %
1.1b	oldMale	youngFemale	-15.04 %
1.2a	oldFemale	youngFemale	-22.76 %
1.2b	oldMale	youngFemale	-12.86 %
2a	youngFemale	youngMale	21.76 %
2b	youngMale	oldFemale	-16.55 %
3a	youngFemale	oldMale	29.99 %
3b	youngMale	oldFemale	-30.01 %

4 Discussion

The definition of appropriate BC for hemodynamic simulations is of particular importance. The study investigates the effect of specific inflow conditions on hemodynamic parameters, which are particularly relevant for risk analysis of intracranial aneurysms [2]. The modeled four inflow curves reflect differences between age and gender groups. The results show that each hemodynamic parameter changes during simulation with a varying inflow curve. Consequently, they are not robust to the varying inflow curves. These findings are in agreement with the study of Detmer et al. [5], where the effect of the inflow BC of CFD simulations are investigated as well. Furthermore, the results also support the findings of Jansen et al. regarding the choice of patient-specific inlet BCs, as there are significant differences in hemodynamic parameters with generalized BCs [7]. Despite the many studies regarding the rupture risks of an aneurysm, there are no generalized defined thresholds for any of the hemodynamic parameters that can classify the aneurysm as being at risk of rupture. However, there are tendencies, that a low WSS and a high OSI might promote rupture [8]. Nevertheless, there are studies, such as by Cerebral et al. [4], which try to define such thresholds based on robust statistical analyses. Exemplarily, in this study, an ICI value for pulsatile flow starting at a value of 1.012 is assigned to a ruptured aneurysm, and an unruptured aneurysm is assigned an average value of 0.66. With the available results, although no change in inflow curves within a case results in an aneurysm being assessed as at risk of rupture for one inflow curve and not for another inflow curve. However, the difference between the values of Cerebral et al. is 0.352. This magnitude of change is even exceeded in four cases, and the variation of the inflow curves may cause a change in the ICI value of up to 1.18. Consequently, a different threshold could result in the aneurysm being considered at risk of rupture with one inflow curve compared with another one. Thus, consideration of patient-specific inflow curves is important for all hemodynamic parameters. Furthermore, patient-specific inflow curves also consider flow data changes due to cardiovascular diseases [6].

Limitations: The presented approach has several limitations. Although a considerable number of over 300 cases of aneurysms were evaluated, only eight cases could be identified for the complex research question. The localization was limited to aneurysms at the Acom to avoid the influence of the localization and keeping the aneurysm site constant. Due to technical limitations and the lack of a direct in vivo blood flow measurement, no ground truth exists. The inflow curves are thus not generated from patient measurements, but are taken from the literature and subsequently modified.

5 Conclusion

The study addresses the influence of different inflow BC on hemodynamic parameters of eight aneurysm cases. While modeling the inflow curves with the patient-specific characteristics, differences between gender and the age of the patients are visible among the different curves. The results of the simulations indicate that all considered hemodynamic parameters are not robust to varying inflow BC. The age difference leads to larger differences than the gender difference for all hemodynamic parameters. Thus, it is recommended to use patient-specific inflow BC in computer-aided simulations of intra-aneurysmal blood flow in research and clinical practice if available, especially for the analysis of potential rupture risks.

Author Statement

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References

[1] Berg P, Beuing O. Multiple intracranial aneurysms: a direct hemodynamic comparison between ruptured and unruptured vessel malformations. Int J Comput Assist Radiol Surg. 2018;13(1):83-93. doi:10.1007/s11548-017-1643-0

[2] Cebral JR, Mut F, Weir J, Putman CM. Association of hemodynamic characteristics and cerebral aneurysm rupture. AJNR Am J Neuroradiol. 2011;32(2):264-270. doi:10.3174/ajnr.A2274

[3] Cebral JR, Castro MA, Burgess JE, Pergolizzi RS, Sheridan MJ, Putman CM. Characterization of cerebral aneurysms for assessing risk of rupture by using patient-specific computational hemodynamics models. AJNR Am J Neuroradiol. 2005;26(10):2550-2559.

[4] Cebral JR, Mut F, Weir J, Putman C. Quantitative characterization of the hemodynamic environment in ruptured and unruptured brain aneurysms. AJNR Am J Neuroradiol. 2011;32(1):145-151. doi:10.3174/ajnr.A2419

[5] Detmer FJ, Mut F, Slawski M, Hirsch S, Bijlenga P, Cebral JR. Incorporating variability of patient inflow conditions into statistical models for aneurysm rupture assessment. Acta Neurochir (Wien). 2020;162(3):553-566. doi:10.1007/s00701-020-04234-8

[6] Durka MJ, Wong IH, Kallmes DF, et al. A data-driven approach for addressing the lack of flow waveform data in studies of cerebral arterial flow in older adults. Physiol Meas. 2018;39(1):015006. Published 2018 Feb 1. doi:10.1088/1361-6579/aa9f46

[7] Jansen IG, Schneiders JJ, Potters WV, et al. Generalized versus patient-specific inflow boundary conditions in computational fluid dynamics simulations of cerebral aneurysmal hemodynamics. AJNR Am J Neuroradiol. 2014;35(8):1543-1548. doi:10.3174/ajnr.A3901

[8] Lv N, Wang C, Karmonik C, et al. Morphological and Hemodynamic Discriminators for Rupture Status in Posterior Communicating Artery Aneurysms. PLoS One. 2016;11(2):e0149906. Published 2016 Feb 24. doi:10.1371/journal.pone.0149906

[9] Vlak MH, Algra A, Brandenburg R, Rinkel GJ. Prevalence of unruptured intracranial aneurysms, with emphasis on sex, age, comorbidity, country, and time period: a systematic review and meta-analysis. Lancet Neurol. 2011;10(7):626-636. doi:10.1016/S1474-4422(11)70109-0

[10] Xiang J, Siddiqui AH, Meng H. The effect of inlet waveforms on computational hemodynamics of patient-specific intracranial aneurysms. J Biomech. 2014;47(16):3882-3890. doi:10.1016/j.jbiomech.2014.09.034

[11] Xu L, Liang F, Zhao B, Wan J, Liu H. Influence of aging-induced flow waveform variation on hemodynamics in aneurysms present at the internal carotid artery: A computational model-based study. Comput Biol Med. 2018;101:51-60. doi:10.1016/j.compbiomed.2018.08.004

[12] Hoi Y, Wasserman BA, Xie YJ, et al. Characterization of volumetric flow rate waveforms at the carotid bifurcations of older adults. Physiol Meas. 2010;31(3):291-302. doi:10.1088/0967-3334/31/3/002