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Relationships and redundancies of selected hemodynamic and structural parameters for characterizing virtual treatment of cerebral aneurysms with flow diverter devices

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ABSTRACT

Background and purpose: To quantify the relationship and to demonstrate redundancies between hemodynamic and structural parameters before and after virtual treatment with a flow diverter device (FDD) in cerebral aneurysms.
Methods: Steady computational fluid dynamics (CFD) simulations were performed for 10 cerebral aneurysms where FDD treatment with the SILK device was simulated by virtually reducing the porosity at the aneurysm ostium. Velocity and pressure values proximal and distal to and at the aneurysm ostium as well as inside the aneurysm were quantified. In addition, dome-to-neck ratios and size ratios were determined. Multiple correlation analysis (MCA) and hierarchical cluster analysis (HCA) were conducted to demonstrate dependencies between both structural and hemodynamic parameters.
Results: Velocities in the aneurysm were reduced by 0.14 m/s on average and correlated significantly ($p < 0.05$) with velocity values in the parent artery (average correlation coefficient: 0.70). Pressure changes in the aneurysm correlated significantly with pressure values in the parent artery and aneurysm (average correlation coefficient: 0.87). MCA found statistically significant correlations between velocity values and between pressure values, respectively. HCA sorted velocity parameters, pressure parameters and structural parameters into different hierarchical clusters. HCA of aneurysms based on the parameter values yielded similar results by either including all ($n=22$) or only non-redundant parameters ($n=2$, 3 and 4).
Conclusion: Hemodynamic and structural parameters before and after virtual FDD treatment show strong inter-correlations. Redundancy of parameters was demonstrated with hierarchical cluster analysis.

1. Introduction

Endovascular treatment utilizing flow diverting devices (FDD) has recently been introduced for cerebral aneurysms (Arrese et al., 2013; Berge et al., 2012; De Vries et al., 2013; Gory et al., 2014; Murthy et al., 2014; Puffer et al., 2014; Takemoto et al., 2014; Zhou et al., 2014). Reported complications include delayed rupture (Karmonik et al., 2013; Mantha et al., 2009) and delayed parenchymal hemorrhage (Tomas et al., 2014). Simulations based on computational fluid dynamics (CFD) techniques have been postulated as an aid for gaining a better understanding of hemodynamics changes induced by FDD (Cebral et al., 2011; Darsaut et al., 2013; Karmonik et al., 2013; Kulcsar et al., 2012; Xu et al., 2013; Zhang et al., 2013), e.g. for obtaining better insights into treatment outcome before the actual intervention, or for identifying if a particular aneurysm is a good candidate for FDD treatment.

To facilitate the use of CFD in clinical research, a research prototype of a dedicated CFD simulation environment was recently introduced where FDD placement is approximated by mathematically reducing the porosity of the aneurysm ostium

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(Karmonik et al., 2013, 2014). This approach represents a simplification of the actual situation where a fine mesh of stent struts is responsible for the flow diversion effect.

As a result of the underlying mathematical assumptions for CFD, it is our hypothesis, that relationships between hemodynamics parameters exist which may introduce redundancies for characterizing virtual FDD treatment outcome. A better understanding of these relations is necessary for assessing the potential of CFD to characterize the hemodynamic state of a particular aneurysm. In this study, we demonstrate these relationships and consequent redundancies for pressure and velocity parameters as well as selected structural parameters, the dome–neck ratio (DNR) and the dome to parent artery radius ratio (DRR), the latter being proportional to the size ratio (SR) (Strother and Jiang, 2012). These structural parameters are of particular interest in FDD treatment as pressure values have been identified to be of interest for aneurysm rupture (Cebral et al., 2011). Velocity values can be directly assessed by non-invasive imaging (Karmonik et al., 2014).

In addition to demonstrate redundancy of hemodynamic parameters, the second purpose of this study was to demonstrate that hierarchical cluster analysis (HCA) provides a means to reduce the large parametric space of hemodynamic (Mihalef et al., 2011) and structural parameters to the most significant subset. This subset is then sufficient to group or classify the investigated aneurysms.

2. Materials and methods

Approval of the local IRB committees was obtained for this retrospective study.

2.1. Computational simulations

Further technical details describing the CFD simulations can be found in Appendix A.1. The solver that was used has been previously described (Mihalef et al., 2011) and validated (Ionasec et al., 2009) and was used to create virtual angiograms based on patient-specific angiographic image data from cerebral aneurysm (Endres et al., 2012). Diagnostic 3D digital subtraction angiography (DSA) data of 10 sidewall aneurysms of the internal carotid artery was imported into a prototype CFD workstation, version 2.0 (prototype Siemens Healthcare GmbH, Forchheim, Germany-not for clinical use). Utilizing a dedicated user interface modeled after clinical 3D visualization software, computational models of all aneurysms were created and two steady simulations, the first without a virtual FDD (PRE) and the second with a virtual FDD (POST), both with a constant inflow of 0.8 m/s and pressure zero at the outlets, were performed for each aneurysm. The velocity of 0.8 m/s was chosen to mimic systolic flow conditions in normal internal carotid arteries (Ford et al., 2005), in order to study FDD effects at maximum inflow into the aneurysm. Only steady simulations were performed as a recent comparison demonstrated good agreement of temporal means for hemodynamic parameters from transient simulations with results of steady simulations (Karmonik et al., 2015). It should be noted that using the same inflow boundary conditions for all cases leads to results, which are governed only by the geometry of the aneurysm models (Xiang et al., 2011) and the parameters characterizing the porous interface. The latter were chosen to correspond to the SILK device (Augsburger et al., 2011). These simulations, therefore, cannot take into account physiological variations of cerebral flows as no flow data from the individual patients was incorporated into the simulations (Xiang et al., 2011). Neither can they make any direct statements to aneurysm rupture risk, as rupture may not be associated with highest flows.

2.2. Hemodynamic and geometrical parameters

The following naming conventions were used to consistently name the hemodynamic parameters: the first letter denotes the physical property (p: pressure, v – velocity, f: flow),the second letter denotes the location: A: aneurysm, P: proximal, D: distal, O: ostium. The last parameter specifies PRE, i.e., native (n) or POST FDD treatment (f), or, in the case of parameters derived for the ostium, the direction of the velocity/flow either into the aneurysm: p (plus) or out of the aneurysm: m (minus). The locations and techniques for extracting the values of these parameters are further illustrated in Fig. 1 and in Appendix A.2. It should be remembered though, that CFD is only able to calculate pressure up to an arbitrary constant. In our setup, outflow pressure was given by the zero pressure boundary condition and inflow pressure was given by the constant inflow velocity. This means, that effectively the pressure drop across the computational model was calculated, which has to be considered when comparing the stated pressure values with values measured in the human circulation.

2.3. Pressure parameters

The following pressure parameters were extracted from the simulations: pressures averaged over the entire aneurysm PRE FDD treatment (pAn) and POST FDD treatment (pAf), pressures in the parent artery proximal PRE and POST FDD treatment (pPn and pPf, respectively) as well as distal to the aneurysm before and after treatment (pDn and pDf, respectively) and pressures in the ostium at the region of inflow and at the region of outflow prior to treatment (pOp and pOm, respectively). The difference in average aneurysm pressure induced by treatment dp was calculated as dp=pAf–pAn.

2.4. Velocity parameters

Analogous to the pressure parameters, values of the following velocity parameters were determined: velocities averaged over the entire aneurysm pre-FDD treatment (vAn) and post-FDD treatment (vAf), velocities in the parent artery proximal PRE and POST FDD treatment (vPn and vPf, respectively) as well as distal to the aneurysm before and after treatment (vDn and vDf, respectively) and velocities in the ostium at the region of inflow and at the region of outflow prior to treatment (vOp and vOm, respectively). The difference in average aneurysm velocity induced by treatment dv was calculated as dv=vAf-vAn.

2.5. Flow parameters

Only the volumetric flow rates into the aneurysm (fOp) and out of the aneurysm after FDD treatment were included as flow changes in the parent artery are expected to be proportional to corresponding velocity changes.

2.6. Geometrical parameters

DRR, proportional by a factor of two to the size ratio (DRR) and DNR were obtained from standard fluoroscopic projection images.

3. Data analysis

For additional technical details of the data analysis please refer to Appendix A.2.

3.1. Multiple correlation analysis

A correlation matrix of all parameters was created to identify statistical significant (statistical significance was defined as $p < 0.05$) relationships between parameters. Parameters that are dependent on each other will introduce redundancy when used to describe the hemodynamic state of a particular aneurysm.

3.2. Hierarchical cluster analysis

Two separate HCA steps were performed. In the first step, the hemodynamic and structural parameters were clustered whereby each parameter was described by its values derived from the simulation result for each aneurysm. Clusters identified in this step will contain each a set of redundant parameters. In contract to MCA introduced on the previous section, moving up in the hierarchy of clusters in the HCA dendogram allows to reduce the parameter set thereby eliminating redundant parameters (i.e. by choosing one representative parameter for each cluster). This is further illustrated in the second HCA step, where all aneurysms were clustered using either the entire parameter set ($n=22$) or reduced sets of $n=4$,3, and 2 with redundant parameters eliminated. Similarity of the obtained aneurysm clusters is then indicative of successfully removing redundant parameters.

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