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Computational flow analysis of the washout of an aortic valve by means of Eulerian transport equation

Abstract: Although the development of the transcatheter aortic valve (TAV) has saved many lives of inoperable patients and has a very good clinical outcome, concerns about valve thrombosis are increasing. Due to the potential risk of late clinically relevant events, the US Food and Drug Administration (FDA) suggests a careful systematic investigation of thrombosis and reduced leaflet motion related to hemodynamic changes induced by TAV implantation. Furthermore, recently published position papers of the ISO working group address numerical and experimental flow field assessment of TAV. In particular, pathologically high shear rates and a reduced washout of the sinuses may increase the risk of valve thrombosis and should therefore be investigated. By means of fluid-structure interaction (FSI) as a powerful *in silico* tool, the transient flow field in an aortic valve was analyzed. A linear elastic behavior was assumed for leaflet material properties (Young modulus: 10 MPa, Poisson ratio: 0.46 and leaflet material density: 1000 kg/m³) and blood was specified as a homogeneous, Newtonian and incompressible fluid (fluid density: 1060 kg/m³ and a dynamic viscosity: 0.0035 Pa s).

In this numerical study we present a Eulerian approach, which is based on transport equation of the residence time (*RT*) as a passively transported scalar. It can be clearly seen that the *RT* is significantly higher in the sinus referred to the main flow. At time step $t = 0.25$ s, the average residence time in the main flow is $RT_{avg} \approx 0.05$ s, whereas $RT \approx 0.25$ s in the sinus. In particular, *RT* is a valuable hemodynamic metric to quantify

the washout of the sinus in order to evaluate the thrombogenic potential of TAV devices. Further studies will concentrate on particle image velocimetry measurements for validation purposes. In particular the velocity in the sinus and therefore the washout is one important hemodynamic key feature that has to be improved for future TAV designs.

Keywords: Washout, residence time, scalar transport, aortic valve

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1 Introduction

Today, surgical aortic valve replacement (SAVR) is the gold standard of treatment for patients with aortic stenosis. Patients with an increased surgical risk are preferably treated by transcatheter aortic valve implantation (TAVI) [1,2]. Currently, in Germany the number of TAVI is twice as high as SAVR [3]. Due to the positive clinical outcome of TAVI in patients with intermediate risk [4], there are extensive ambitions to expand the indication of TAVI to lower risk patients [5].

Particularly, the occurrence of valve thrombosis is associated with reduced leaflet motion and flow stagnation in the sinuses [6-8]. These findings trigger concerns regarding an increased risk of stroke and the limitation of long-term valve durability [9]. The mechanisms leading to thrombosis in the cardiovascular system are traditionally described by means of Virchow's triad [10]: hemodynamic factor (fluid stasis and/or high shear stresses), surface factor (endothelial injury, leaflet damage), and hemostatic factor (hypercoagulability, significant tissue injury) [7,11].

In particular, the hemodynamic situation in the sinuses of the valve prosthesis, which is characterized by recirculation, low fluid velocity and therefore high residence time (*RT*), is a critical factor in the development of valve thrombosis [9].

Hemodynamic analysis (e.g. wall shear stress and shear rate distribution) by means of computational fluid dynamics (CFD) of cardiovascular implants can substantially augment the knowledge obtained from *in vitro* and *in vivo* studies.

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Currently, there is no standard approach for the CFD assessment of transcatheter heart valve prostheses available. To overcome this limitation, the ISO working group has drafted a position paper, which provides guidance for performing CFD analysis [12]. Of special interest is the calculation of the washout time.

By using a Lagrangian method, the behavior of individual blood cells and therefore RT within the sinuses can be modelled. However, extensive computational costs are required.

In this numerical study we present a Eulerian method, which is based on transport equation of RT as a passively transported scalar [13,14]. This approach allows for the calculation of RT without high computational effort.

2 Materials and methods

2.1 Aortic valve model

The aortic valve model used in this study was formerly proposed by Pfensig et al. and consists of a generic aortic root with three identical leaflets [15]. Geometrical parameters are based on studies by Reul et al. [16]. The aortic valve model was created by means of Creo Parametric 3.0 (Parametric Technology Corp., Needham, MA, USA). A segment of the discretized computational domain is depicted in Figure 1. Calcification of the leaflets and other pathological alterations of the geometry as well as the material properties were neglected

Figure 1: Segment of the discretized computational domain. Due to symmetry only one third of the aortic valve was simulated. The contour of the leaflet is colored yellow.

2.2 Fluid-Structure Interaction

For physiologically accurate simulations, the fluid flow through the valve and the leaflet motion should be modelled simultaneously. The principle of fluid-structure interaction (FSI) is to model both: fluid dynamics and structural mechanics, which are coupled by an interface. The mesh deformation was realized using the arbitrary Lagrangian-Eulerian (ALE) method implemented in ANSYS 18.0.

A linear elastic behavior was assumed for leaflet material properties (Young modulus: 10 MPa, Poisson ratio: 0.46 and leaflet material density: 1000 kg/m³) and blood was specified as a homogeneous, Newtonian and incompressible fluid (fluid density: 1060 kg/m³ and dynamic viscosity: 0.0035 Pa s) [17]. In a further step, the geometrical configuration as well as the flow field of the FSI-modeled valve prosthesis was used for RT simulation in a quasi-steady state manner.

2.3 Residence time RT

RT is used to quantify regions of stagnancy, flow recirculation as well as the sinus washout, which are associated with an increased likelihood for thrombus formation [14]. RT is the time that a certain particle has spent since entering the computational domain [13]. Several numerical and experimental approaches have been developed to analyze the blood flow in combination with RT through cardiovascular implants, such as transcatheter heart valves prostheses or stents. In order to evaluate RT of the fluid, some authors propose a particle-based method, which utilizes the Lagrangian frame of reference. This Lagrangian method can be applied to *in vitro* or *in silico* studies. Midha et al. performed particle tracking as a post-processing routine of time-resolved particle image velocimetry measurements to assess the washout time [18].

As a part of CFD analysis the so-called Euler-Lagrange approach can be used to model properties of individual particles, such as RT of blood cells [19]. These studies, whether numerical or experimental, consider blood as a suspension, which is a physiological assumption. Therefore, particle-based methods seem to be the proper choice for RT simulation. But the results depend on the number of particles and their trajectories. It is therefore possible that the region of interest is not covered by enough particles to calculate a statistically valid RT [12].

Additionally, the feasibility of the Lagrangian method as a part of CFD is limited due to the extremely high computational cost and therefore is insufficient to analyze the entire fluid flow [13].

By using the Eulerian frame of reference the entire flow field can be considered with lower computational costs. For example Midha et al. analyzed the velocity field to identify potential stagnation zones within the neosinus. Furthermore, the maximum velocity experienced by each spatial location throughout the entire cardiac cycle was plotted to characterize the washout [18]. Despite the excellent work of Midha et al. there is a missing link between the proposed Eulerian approach and the local RT to quantify the washout in the aortic sinuses.

As a solution we implemented the transport equation for RT , which was proposed by Ghirelli and Leckner (2004), in a custom made solver [13]. RT is modelled as a scalar passively transported with the velocity field [14]:

$$\frac{\partial RT}{\partial t} + v \cdot \nabla RT = D_{RT} \nabla^2 RT + 1$$

where t is time, v represents the velocity of blood, D_{RT} is the self-diffusivity of blood ($D_{RT} = 1.14 \cdot 10^{-11} \text{ m}^2/\text{s}$ [14]). The source term leads to an increase of RT corresponding to the running time.

3 Results and discussion

The flow field in the aortic sinus at $t = 0.25 \text{ s}$ is illustrated by streamlines for topological analyses, see Figure 2A. It can be seen that the blood passes from the main flow to the sinus in the middle of the leaflets. In the area of the leaflet attachments, the blood flow exits from the sinus, resulting in a large vortex structure. It has to be noted that the velocity magnitude in the sinus is below 0.05 m/s . Furthermore, a highly rotating vortex can be detected at the free edge of the leaflet.

The low velocities in the sinus have an effect on the residence time RT . To visualize this effect Figure 2B depicts the same streamlines colored by RT . It can be clearly seen that the RT is significantly higher in the sinus referred to the main flow. The average residence time in the main flow is $RT_{avg} \approx 0.05 \text{ s}$, whereas $RT \approx 0.25 \text{ s}$ in the sinus.

The calculation of RT for the entire computational domain represents the major advantage of the Eulerian approach. Figure 3 depicts RT in a longitudinal section. The influence of the recirculation in the vicinity of the free edge of the leaflet on the mixture of the main flow and blood volume in the sinus is clearly visible.

Figure 2: Numerical simulation of the hemodynamic situation in the aortic sinus; visualization of the flow field by streamlines coloured by velocity magnitude (A) and streamlines colored by residence time RT (B)

Figure 3: Numerical calculated residence time RT in a longitudinal section of an aortic valve

4 Conclusion

The hemodynamic situation in the aortic sinus, which is characterized by recirculation and low velocities or even stasis, is a critical factor in the development of valve thrombosis. According to ISO 5840 a computational flow analysis of TAVI devices should include an evaluation of the thrombogenic potential based on estimations of the washout time, recirculation and separation. We implemented a transport equation for RT as a passively transported scalar, which was formerly proposed by [13]. It could be shown that the residence time in the sinuses is significantly higher compared to the main flow. In contrast to particle-based methods, the implemented transport equation is capable to model RT of the entire domain due to an Eulerian approach. This study is limited to the simulation of the aortic valve. Further studies will concentrate flow simulation of TAVI. In particular, RT is a valuable hemodynamic metric to quantify the washout of the sinus in order to evaluate the thrombogenic potential of TAVI devices.

Author Statement

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References

- [1] Adams DH, Popma JJ, Reardon MJ et al. Transcatheter aortic-valve replacement with a self-expanding prosthesis. *N. Engl. J. Med.* 2014;370(19): 1790-98.
- [2] Thyregod HG, Steinbrüchel DA, Ihlemann N, et al. Transcatheter versus surgical aortic valve replacement in patients with severe aortic valve stenosis. *JACC.* 2015;65(20):2184-94.
- [3] Brucknerberger E. Herzbericht 2018. 30. Bericht. Sektorenübergreifende Versorgungsanalyse zur Kardiologie in Deutschland sowie vergleichende Daten zur Kardiologie aus Österreich und der Schweiz. Hannover 2018.
- [4] Tamburino C, Barbanti M, D'Errigo P, et al. 1-Year outcomes after transfemoral transcatheter or surgical aortic valve replacement. *J. Am. Coll. Cardiol.* 2015; 66(7):804-12.
- [5] Gravel, G. M., and P. Gnreux. Exploring the role of transcatheter aortic valve replacement as the preferred treatment for lower-risk patients. *JACC.* 2015;66(14):1638-39.
- [6] Egbe AC, Pislaru SV, Pelikka PA, et al. Bioprosthetic valve thrombosis versus structural failure: clinical and echocardiographic predictors. *J Am Coll Cardiol* 2015; 66:2285-94.
- [7] Dansas GD, Weitz JI, Giustino G, Makkar R, Mehran R. Prosthetic Heart Valve Thrombosis. *JACC.* 2016;68(24): 2670-89
- [8] Zoghbi WA, Chambers JB, Dumesnil JG, et al. Recommendations for evaluation of prosthetic valves with echocardiography and Doppler ultrasound. *J Am Soc Echocardiogr.* 2009; 22:975-1014.
- [9] Laschinger JC, Wu C, Ibrahim NG, Shuren JE. Reduced Leaflet Motion in Bioprosthetic Aortic Valves-The FDA Perspective. *N Engl J Med.* 2015; 373(21):1996-98.
- [10] Virchow R. Gesammelte Abhandlungen zur wissenschaftlichen Medizin. Frankfurt: Medinger Sohn & Co., 1856:219-732.
- [11] Wolberg AS, Aleman MM, Leiderman K, Machlus KR. Procoagulant Activity in Hemostasis and Thrombosis: Virchow's Triad Revisited. *Anesth Analg* 2012; 114:275-85.
- [12] Wei ZA, Sonntag SJ, Toma M, et al. Computational Fluid Dynamics Assessment Associated with Transcatheter Heart Valve Prostheses. *Cardiovasc Eng Technol* 2018;9(3):289-99.
- [13] Ghirelli F and Leckner B. Transport equation for the local residence time of a fluid. *Chem Eng Sci.* 2004; 59(3):513-23.
- [14] Menichini C, Xu XY. Mathematical modeling of thrombus formation in idealized models of aortic dissection: initial findings and potential applications. *J. Math. Biol.* 2016; 73(5):1205-26.
- [15] Pfensig S, Kaule S, Smann M, et al. Assessment of heart valve performance by finite-element design studies of polymeric leaflet-structures. *CDBME* 2017;3(2):631-634.
- [16] Reul H, Vahlbruch A, Giersiepen M, et al. The geometry of the aortic root in health, at valve disease and after valve replacement. *J. Biomechanics* 1990; 23(2):181-191.
- [17] Borowski F, Smann M, Pfensig S, et al. Fluid-structure interaction of heart valve dynamics in comparison to finite-element analysis. *CDBME* 2018; 4(1): 259 - 262.
- [18] Midha PA, Raghav V, Sharma R, et al. The Fluid Mechanics of Transcatheter Heart Valve Leaflet Thrombosis in the Neosinus. *Circulation.* 2017; 136:1598-1609.
- [19] Vahidkhah K, Barakat M, Abbasi M, et al. Valve thrombosis following transcatheter aortic valve replacement: significance of blood stasis on the leaflets. *Eur J Cardiothorac Surg* 2017; 51:927-3.