SCUOLA DI INGEGNERIA INDUSTRIALE E DELL'INFORMAZIONE

Executive Summary of the Thesis

Computational hemodynamics for pulmonary valve replacement by means of a reduced Fluid-Structure Interaction model

Laurea Magistrale in Biomedical Engineering - Ingegneria Biomedica

Author: Elisabetta Criseo

Advisor: Prof. Christian Vergara

Co-advisors: Dr. Ivan Fumagalli, Stefano Maria Marianeschi, MD

Academic year: 2021-2022

1. Physiology of the pulmonary circulation

This thesis is a patient-specific study on the pulmonary artery haemodynamics before and after pulmonary valve replacement. Due to the focus of this work, we concentrate on the description of pulmonary circulation and pulmonary valve dynamics.

The pulmonary circulation involves the flowing of blood from the right atrium to the pulmonary arteries. In particular, the right atrium (RA) collects unoxygenated blood from the vena cava. Then blood flows from the right atrium to the right ventricle (RV), passing through the tricuspid valve (TV) and is ejected through the pulmonary valve (PV) into the pulmonary artery; finally it is transported through pulmonary capillaries and oxygenated blood is obtained by gas exchange in the alveolae [4].

The ejection of blood through the PV follows the phases of the cardiac cycle. Specifically, during systole the heart muscle is contracted, the PV is open and the ejection of blood from the RV to the pulmonary artery takes place; the diastole instead coincides with the relaxation of the heart muscle, the PV is closed whereas the TV is open and the right ventricle is filling.

Pulmonary valve dynamics, are governed by the force balance computed at the interface between the blood and the valve leaflets. The main forces contributing to the balance are internal elastic forces and fluid forces acting on the valve surface.

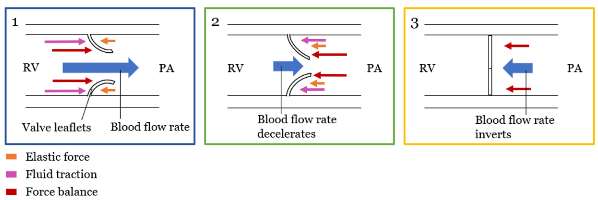

Figure 1: The phases describing pulmonary valve dynamics.

Specifically (Figure 1):

- During the systole, the fluid force acts on the leaflets, exceeding the opposing elastic force and causing the leaflets to open.
- After the opening of the leaflets, the fluid force inverts, adding up to the elastic force, so the force balance is inverted. Accordingly, the valve closure begins while the flow rate decelerates.
- As the systole is ending, the flow rate tends

to reverse, however, the force balance drives the valve closure, impeding the generation of a flow going upstream the valve.

2. The case study

The two patients considered for this work were affected by Tetralogy of Fallot (TOF), a congenital heart disease characterised by the presence of a tetrad of anatomical heart anomalies: a ventricular septal defect, the obstruction of the right ventricle outflow tract, overriding of the aorta and right ventricular hypertrophy [1].
In the case of our patients, a defect to the aortic valve added up to this tetrad of anomalies. Thus, after the repair of TOF, the patients underwent the Ross procedure, i.e. the substitution of the aortic valve with an autograph, namely their pulmonary valve; at this point, the patients' pulmonary valve was absent.
Clinical evidence showed that this surgery left the patients with significantly pulmonary valve regurgitation; meaning that a consistent fraction of the blood volume ejected by the right ventricle was not reaching the pulmonary circulation due to the establishment of a backflow. Specifically, this last condition caused the patients' right ventricle enlargement, followed by negative repercussions on its functionality.

Figure 2: The No-React® BioPulmonic™

To correct this condition, the two patients underwent the implantation of a stented pulmonary valve at *Niguarda Hospital* in Milan. The valve used is the the *No-React® BioPulmonic™*, which is constituted by a porcine pulmonary valve covered with a bovine pericardium sleeve; these two elements are then mounted on a Nitinol stent which is self-expansible [3].

3. Aim of the work

The aim of this thesis is to analyse the haemodynamics in the pulmonary artery using a computational model to reproduce them before and after the replacement of the pulmonary valve with a stented bioprosthesis.
The analysis will comprehend the simulation of three scenarios for each patient:

1. A pre-operative scenario, characterised by pulmonary valve regurgitation.
2. A post-operative scenario, describing the patients' condition 6 months after the pulmonary valve replacement.
3. A follow-up scenario, describing the patients' condition 9 years after the pulmonary valve replacement.

To implement these, the following models have been adopted:

- A closed-0D model of the whole cardiovascular system.
- A 3D Computational Fluid Dynamics (CFD) model for the pre-operative scenario.
- A reduced Fluid-Structure Interaction (FSI) model which employs the Resistive Immersed Implicit Surface (RIIS) method for the valve modelling, in the post-operative and follow-up scenarios.

The post-operative and follow-up scenarios are described using the same geometry and reduced FSI model: their differences lay in the boundary conditions applied.
Since most of the studies on cardiac valve replacement concentrate on the aortic valve, this study could give an additional point of view in the analysis of pulmonary circulation and prosthetic pulmonary valve dynamics.
The main novelties with respect to previous studies on pulmonary artery haemodynamics are the use of a reduced FSI model, instead of a diode-like model for the pulmonary valve, and the calibration of the 0D model of the circulation to reproduce the patients' clinical status; thus, the boundary conditions imposed to the 3D models are patient-specific.

4. Imaging and preprocessing

The computational domains used in this thesis are patient-specific, indeed they were segmented and reconstructed starting from the patients' CT acquisitions.
Since pulmonary valve replacement affects the haemodynamics mainly in the pulmonary trunk and in proximity of the first bifurcation, during the reconstruction process the geometry was cut in order to obtain one inlet and two outlets, corresponding to the two main branches outlets.

For the pre-operative scenario, the geometry was not further modified. Instead, in the post-operative and follow-up scenarios, a cylinder modelling the pericardial sleeve of the stented valve was included in the model. In this way, it was possible to differentiate the scenarios modelling the condition before and after the pulmonary valve replacement starting from the computational domain.
In the post-operative and follow up scenarios the presence of the valve must be accounted for. The geometry of the pulmonary valve was obtained starting from a model by Zygote, since the CT acquisitions had a poor resolution which did not allow the leaflets reconstruction.
This valve model was adapted to fit properly the pulmonary artery geometry. Moreover, the open configuration of the valve was obtained and the displacement from the closed configuration to the open one was reconstructed.
Finally, starting from the geometries reconstructed, tetrahedral meshes were obtained.

5. Mathematical models

In this thesis a geometric multiscale approach was adopted, meaning that a 3D model was used to describe only the region of interest, namely the pulmonary artery, whereas the rest of the circulation is modeled by means of a reduced model [5].
Lumped Parameters Model of the Whole Circulation. This model allows to reproduce both the systemic and pulmonary circulations in a simplified way, providing, however, reliable measures of fluid dynamic quantities at a systemic level.
In this application, the lumped parameters model has been used in order to extract the pressure dynamics at the right ventricle and at the pulmonary artery level. These are prescribed as boundary conditions (BCs) to the 3D model, at the inlet and the two outlets, respectively.
The cardiovascular system is divided into compartments, which are described using time-dependent variables through a set of ordinary differential equations (Figure 3).
The model chosen for the pulmonary valve is a non-ideal diode, whose behaviour is described by R_{max}, the resistance opposing the flow when the valve is closed, and R_{min} when it is open.
Depending on the values chosen for R_{min} and R_{max}, two models were defined:

- Pre-0D model: used for the BCs of the pre-operative scenario; in this case $R_{max} \simeq R_{min}$, so the model simulates a situation in which the valve is absent.
- Valve-0D model: used for the post-operative and follow-up scenarios BCs; the model reproduces the haemodynamics after pulmonary valve replacement. In this case $R_{max} \gg R_{min}$, so the valve model simulates the behaviour of a healthy valve.

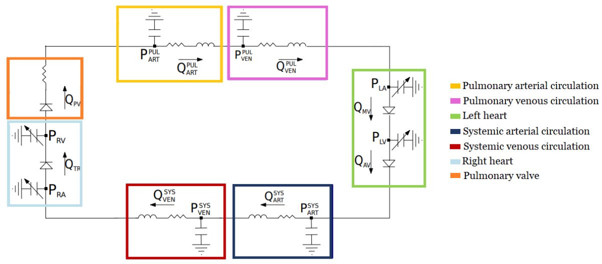

Figure 3: The lumped parameters model of the whole circulation.

Pre-operative fluid model. Two different 3D models were used: the first describes the pre-operative scenario and does not include the interaction between the blood and the valve leaflets, since the patients in this scenario did not have the pulmonary valve. Moreover, the assumption of rigid wall is made. Thus, in the pre-operative scenario the mathematical model does not take into account any fluid-structure interaction.
Since the blood, in all the models, is described as an incompressible homogeneous Newtonian fluid [4], with density $\rho = 1.06 \cdot 10^3\, kg/m^3$ and dynamic viscosity $\mu = 3.5 \cdot 10^{-3}\, Pa \cdot s$, the problem is described by the Navier-Stokes equations for an incompressible homogeneous Newtonian fluid in Ω_{pre} (see Figure 4).

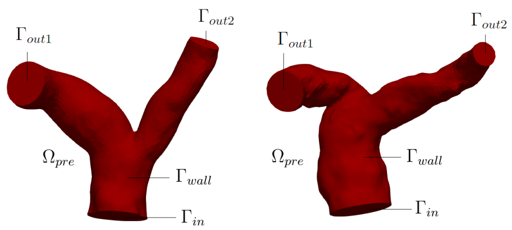

Figure 4: Patient's 1 and 2 computational domain in the pre-operative scenario.

In particular, on the artificial boundaries Γ_{in}, Γ_{out_1}, Γ_{out_2} Neumann boundary conditions are applied. On the physical boundary of the pulmonary artery geometry Γ_{wall}, a no-slip condition is applied. Finally, null velocity is the initial condition of the model.

Post-operative/follow-up scenarios reduced FSI model. The second 3D model describes both the post-operative and follow-up scenarios; indeed, in both cases the fluid-structure interaction between the blood and the stented valve leaflets is modeled. As in the pre-operative scenario, the assumption of rigid wall is made.

The problem is described by the formulation of Navier-Stokes equation for an incompressible, homogeneous, Newtonian fluid in Ω_{pvr} (Figure 5). Also in these scenarios, Neumann boundary conditions are applied on the artificial boundaries Γ_{in}, Γ_{out_1}, Γ_{out_2}. On the physical boundary of the pulmonary artery geometry Γ_{wall}, a no-slip condition is applied. Finally, null velocity is the initial condition of the problem.

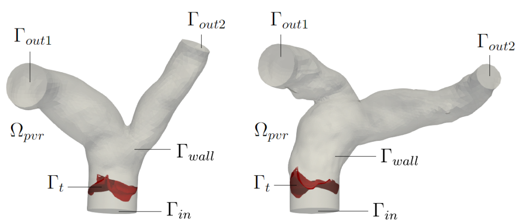

Figure 5: Patient's 1 and 2 computational domain for the post-operative and follow-up scenarios.

The interaction of the valve is considered by adopting the Resistive Immersed Implicit Surface (RIIS) method as in [2], so by adding the term $\frac{R}{\varepsilon}(\mathbf{u} - \mathbf{u}_\Gamma)\delta_{t,\varepsilon}$ to the momentum conservation equation of Navier-Stokes formulation. This term is a resistive penalty term which weakly enforces the adherence of the fluid velocity to the leaflets velocity in proximity of the valve surface. Specifically, notice that $\mathbf{u}_\Gamma$ and $\delta_{t,\varepsilon}$ are unknowns and have to be found using the reduced structure model of the valve.

In this model $\mathbf{u}_\Gamma$ is the valve velocity and $\delta_{t,\varepsilon}$ is as a smeared delta Dirac function. This function has support on a narrow layer (identified by the leaflets semi-thickness ε) around the valve surface Γ_t and it is a function of $\varphi_t(\mathbf{x})$, a signed distance function describing the configuration of the valve leaflets.

In particular, the valve surface is described as:

$$\Gamma_t = \{\mathbf{x} \in \mathbb{R}^3 \ : \ \mathbf{x} = \mathbf{T}_t(\widehat{\mathbf{x}}) = \widehat{\mathbf{x}} + \mathbf{d}_\Gamma(t, \widehat{\mathbf{x}})\}.$$

where $\mathbf{d}_\Gamma$ is the displacement of the points in Γ_t with respect to the reference configuration $\widehat{\Gamma}$.

The valve structural model is based on the force balance at the leaflets surface, which reads:

$$\rho_\Gamma \ddot{\mathbf{x}} + \beta \rho_\Gamma \dot{\mathbf{x}} = \mathbf{f}(t, \mathbf{x}) - \gamma[H(\mathbf{x}) - \widehat{H}(\widehat{\mathbf{x}})]\mathbf{n}_\Gamma(\mathbf{x})$$

where the forces acting on the leaflets are the fluid traction forces $\mathbf{f}(t, \mathbf{x})$ and the internal elastic forces of the leaflets, related to their curvature H.

The reduced FSI model is obtained by using a 0D structural model for the valve, in which the displacement is decomposed as a product of two functions:

$$\mathbf{d}_\Gamma(t, \widehat{\mathbf{x}}) = c(t)\mathbf{g}(\widehat{\mathbf{x}}),$$

where $\mathbf{g}$, the valve opening field, is known (obtained in the reconstruction process) and c, the valve opening coefficient, is an unknown.

The coupling between the fluid and structure is carried out by expressing the fluid-to-valve stress $f(t, \boldsymbol{x})$ in terms of the blood velocity $\boldsymbol{u}$ and pressure p. Moreover, the leaflets velocity $\boldsymbol{u}_\Gamma$ and the signed distance function φ_t have to be expressed in terms of c and $\boldsymbol{g}$. This allows the exchange of information from the fluid 3D model to the 0D valve model.

Indeed, the solution of the 0D valve structural problem, allows to find the leaflets velocity $\boldsymbol{u}_\Gamma$, as a function of the displacement, and the smeared Dirac delta $\delta_{\Gamma,\varepsilon}$. These are then passed on to the fluid 3D problem, whose solution allows to obtain the fluid force $\boldsymbol{f}$ acting on the leaflets.

6. Numerical approximation

To solve the problem the mathematical models described in the previous section are discretised both in time and space. Specifically:

- The circulation lumped parameters model is discretised in time using the 4th order Runge-Kutta Method.
- Both the 3D models, CFD and reduced FSI, are discretised in time by using the Backwards Differentiation formula (BDF) of order 1, adopting a semi-implicit treatment

for the non-linear term of the momentum equation in Navier-Stokes formulation.

- Both the 3D models, CFD and reduced FSI, are discretised in space by means of the Finite Element (FE) method, in which the velocity and pressure are expressed using Lagrangian polynomial basis functions of equal first degree.
- The ODE describing the 0D valve model, used in the reduced FSI approach, is solved using the 4th order Runge-Kutta method.

Since, in the space discretisation of the models, finite elements of the same order were used, the SUPG-PSPG stabilisation method was applied to avoid the numerical instabilities caused by the violation of the inf-sup condition. Moreover, backflow stabilisation was applied at the outlets of the computational domain and the sigma-LES turbulence model was adopted to verify if the insertion of the valve generates turbulence.
The linear systems corresponding to the discretisations of the CFD and reduced FSI models were solved using the GMRES algorithm, with a SIMPLE preconditioner. The numerical time step used was $\Delta t = 5\ 10^{-4}$, with a heartbeat period $T = 0.8\ s$.

7. Calibration of the circulation and valve models

First, the lumped parameters model of the whole circulation was calibrated using the available clinical data, i.e. clinical measurements of Patient's 1 heart function. This allowed to extract three different pressure sets to be used as patient-specific boundary conditions for each scenario considered, differentiating them.
The calibration was carried out by fitting the the Ejection Fraction (EF) calculated by the model to the clinical data of Patient 1. The measurements of EF were performed 6 months and 9 years after the pulmonary valve replacement, corresponding to the post-operative and follow-up scenario respectively. As for the pre-operative scenario, the reference values used were the measurements taken 6 months after the surgery; indeed, as observed in literature, the EF has a negligible change if the data from the pre-operative condition and 6 months after the surgery are compared.
The use of the lumped parameters model allowed to reproduce the clinical measured EF with a difference of 10% in the post-operative scenario and 12.5% in the follow-up. The boundary conditions obtained for Patient 1, were then generalised also to Patient 2.
In Figure 6, we summarise the models and data used for each scenario.

	Pre-operative	Post-operative	Follow-up
Geometry	absent valve	pericardial sleeve virtually inserted, valve included	pericardial sleeve virtually inserted, valve included
3D model	CFD model	reduced FSI model	reduced FSI model
Data used for circulation LPM calibration	6 months after PV replacement	6 months after PV replacement	9 years after PV replacement
BC from	Pre-0D model (absent valve)	Valve-0D model (valve included)	Valve-0D model (valve included)

Figure 6: A summary of the models and data used in each scenario considered, both for Patient 1 and Patient 2.

Another calibration was performed for the reduced valve model in the post-operative and follow-up scenarios. The aim of the calibration was to obtain pulmonary valve dynamics characterised by opening and closing times similar to the ones found in literature.

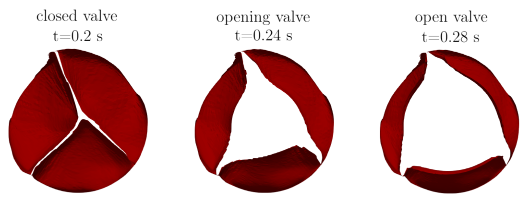

Figure 7: The pulmonary valve opening dynamics reproduced by the reduced FSI model in Patient's 2 follow-up scenario.

The results of the valve calibration were evaluated by analysing the opening coefficient of the valve, calculated by the reduced FSI numerical simulations; an example of the valve opening is shown in Figure 7. The calibration was conclusive in three scenarios over four; indeed, in Patient's 2 post-operative scenario, the valve model was not able to reproduce the valve closure.

8. Results: analysis and discussion

From the analysis of the 3D simulations results, we were able to observe the establishment of a backflow in the pre-operative scenario and the

reduction of the regurgitant fraction in the post-operative and follow-up scenarios, as expected. Specifically, comparing the pre-operative and follow-up scenarios, the regurgitation fraction was reduced by 25.3% in Patient 1 and 22.5% in Patient 2. Moreover, from the study of flow rate, we could also verify that the insertion of the prosthetic valve does not influence the flow distribution in the two main artery branches with respect to the pre-operative scenario.
The use of a patient-specific geometry allowed to visualise how the positioning of the stented valve and patients' geometries influence the haemodynamics of the pulmonary valve. This can be clearly seen in the velocity profile plots (Figure 8) in the moment of the maximum ejection of the flow.

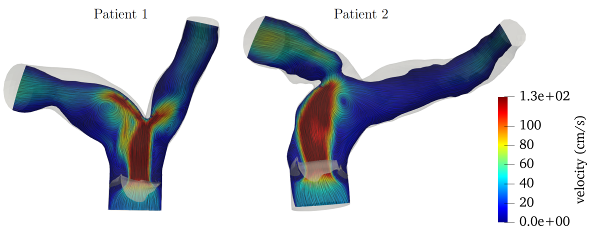

Figure 8: The velocity profiles calculated in the 3D simulations of Patient's 1 (left) and Patient's 2 (right) follow-up scenario at time t=0.34 s.

Indeed, during the systolic peak, a jet of fluid is generated and, due to the different positioning of the stent, the jet hits the artery wall differently in Patient 1 than in Patient 2.
This has a correspondence also in the plots of the WSS (Figure 9) at the same instant, which show the generation of high shear stresses on the pulmonary artery wall in the regions hit by the blood jet.

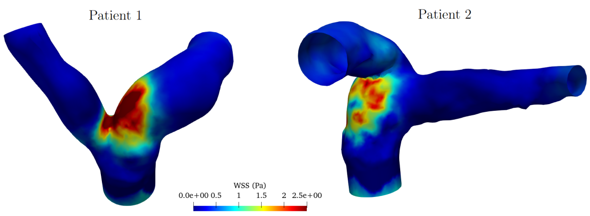

Figure 9: The WSS on the pulmonary artery calculated in the 3D simulations of Patient's 1 (left) and Patient's 2 (right) follow-up scenario at time t=0.34 s.

The insertion of the stented valve puts in evidence also the formation of turbulence near the valve during its closure. Indeed, a backflow is established and the blood flows at high velocity towards the valve surface.
This can be observed in the plots of the ratio between the turbulent viscosity μ_{sgs} (calculated by the sigma-LES model), and the physical viscosity μ. This parameter takes on high values even right after the valve insertion in the post-operative scenario for both Patients (Figure 10).

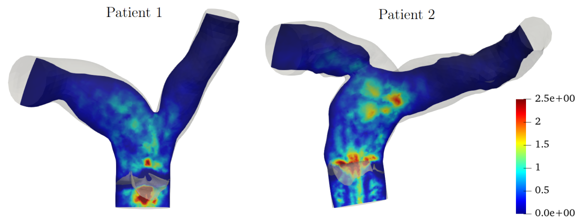

Figure 10: The ratio μ_{sgs}/μ calculated in the 3D simulations of Patient's 1 (left) and Patient's 2 (right) post-operative scenario at time t=0.58 s.

Finally, the analysis of the pressure plots allows to visualise the obstacle offered by the valve when it is closed. Specifically, differently from the pre-operative scenario, the pressure gradient after the valve insertion develops almost exclusively in the proximity of the valve. For example, this is evident in Figure 11.

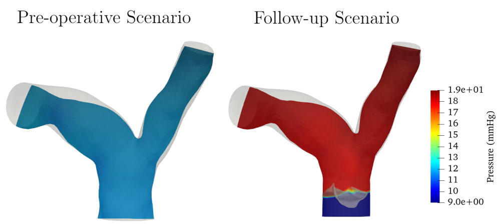

Figure 11: The pressure plots calculated in the 3D simulations of Patient's 1 pre-operative and follow-up scenarios at time t=0.58 s.

9. Limitations and future developments

In this thesis, we were able to simulate the pulmonary artery haemodynamics before and after pulmonary valve replacement, however we can identify some limitations of this work:

- The failed calibration of the valve model in Patient's 2 post-operative scenario allows to point out the limitation represented by the lack of clinical data. Indeed, having Patient's 2 clinical measurements would have allowed to apply patient-specific BCs as for Patient 1, avoiding the generalisation made.

- The models used for the reproduction of pulmonary artery haemodynamics neglect the deformation of the pulmonary artery.
- The valve and stent geometry used was not recontructed from the CT acquisitions of the patients analysed, limiting the patient-specificity of the model.

Future developments of this study could concern:

- A more extensive study on the calibration of the valve model.
- The coupling of the 3D model of the pulmonary artery with the lumped parameters model of the circulation.
- The influence of the stented valve positioning on the flow patterns established after pulmonary valve replacement.
- A more extensive study, collecting more patient-specific models, in order to analyse the different outcome of the study with respect to the geometry of the pulmonary artery considered or to the different boundary conditions used.

References

[1] C. Apitz, G. D. Webb, and A. N. Redington. Tetralogy of Fallot. *The Lancet*, 374:1462–1471.

[2] I. Fumagalli. A reduced 3D-0D FSI model of the aortic valve including leaflets curvature. *arXiv preprint arXiv:2106.00571*, 2021.

[3] S. Ghiselli, C. Carro, N. Uricchio, G. Annoni, and S. M. Marianeschi. Mid-to long-term follow-up of pulmonary valve replacement with biointegral injectable valve. *European Journal of Cardio-thoracic Surgery*, 59:325–332, 2 2021.

[4] A. Quarteroni, A. Manzoni, and C. Vergara. The cardiovascular system: Mathematical modelling, numerical algorithms and clinical applications. *Acta Numerica*, 26:365–590, 5 2017.

[5] A. Quarteroni, A. Veneziani, and C. Vergara. Geometric multiscale modeling of the cardiovascular system, between theory and practice. *Computer Methods in Applied Mechanics and Engineering*, 302:193–252, 4 2016.