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Fluid-Structure Interaction Assessment of Blood Flow Hemodynamics and Leaflet Stress During Mitral Regurgitation

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Abstract

The aim of this study is to simulate the Mitral Regurgitation (MR) disease progression from mild to severe intensity. A Fluid Structure Interaction (FSI) model was developed to extract the hemodynamic parameters of blood flow in mitral regurgitation (MR) during systole. A two-dimensional (2D) geometry of the mitral valve was built based on the data resulting from Magnetic Resonance Imaging (MRI) dimensional measurements. The leaflets were assumed to be elastic. Using COMSOL software, the hemodynamic parameters of blood flow including velocity, pressure, and Von Mises stress contours were obtained by moving arbitrary Lagrange-Euler mesh. The results were obtained for normal and MR cases. They showed the effects of the abnormal distance between the leaflets on the amount of returned flow. Furthermore, the deformation of the leaflets was measured during systole. The results were found to be consistent with the relevant literature.

Keywords: Fluid-Structure Interaction, hemodynamics, mitral, regurgitation, systole

Introduction

Mitral valve regurgitation is a condition in which the valve does not close tightly and there is an abnormal reversal of blood flow from the left ventricle to the left atrium. This increases the pressure in the left atrium and may lead to complications such as dyspnea, fatigue, orthopnea, and pulmonary edema. Mitral valve regurgitation is an important health issue. More than three millions people in the USA suffer from moderate or severe regurgitation [1]. In spite of the fact that measuring hemodynamic parameters in left ventricle and mitral valve stress patterns are significantly challenging, numerical analyses can be used to develop new models to further understand this issue [2]. Coincident with developments in non-invasive blood flow imaging (echo-doppler and Magnetic Resonance Imaging, MRI), in recent years significant studies have combined such imaging with numerical simulation [3]; with applications to human mitral valves, including prediction of disease progression and treatment.

One of the first attempts for modeling of mitral regurgitation (MR) was by Dent et al. [4] who introduced a mathematical model for the quantification of MR using experimental data. In parallel, Doppler echocardiography, color Doppler assessment, and color Doppler mapping were used to study the degree of MR [5,6,7]. More recently, Wenk et al. [8] have studied a finite element model of the left ventricle with mitral valve. Their model was based on magnetic resonance imaging data from a sheep that had developed moderate ischemic MR after postero-basal myocardial infarction. A three-dimensional (3D) FSI model of MR flow was presented by Mao et al. [9] that showed the FSI method could simulate the coupled valves structure response and the intraventricular hemodynamics in left ventricle. Little et al [10] introduced a 3D ultrasound imaging model of MR. Einstein [11] studied MR by using a Fluid-Structure Interaction (FSI) model.

Together these studies have presented a comprehensive strategy for analyzing MR. Development by This et al. [12] presented a one-way FSI model to simulate three different mitral valve defects, including blood-flow in patients. While numerical techniques, including FSI, have been applied for the development of a ‘healthy’ mitral valve model [13-15], Su et al. [16] studied the intraventricular flow in a patient-specific mitral and aortic valves integrated model including left ventricle using a Two-dimensional methodology. Their results confirmed the ability of estimating the patient-specific intraventricular flow by means of numerical method together with FSI approach. While models of MR are developing, there has been limited assessment of the effect of ventricular and annular dimensions on MR. Particularly valuable is intraventricular flow during the early diastolic phase, when the hemodynamic parameters including vortices may be important in filling [17], closure and regurgitation of the mitral valve.

The aim of this study is the development of a computational model for the assessment of MR, including its progression from mild to severe. To assess the feasibility of developing such an FSI model, a 2D model is assessed, which may also be more likely to undergo clinical translation due to the model solution times [3]. This initial model has focused on assessing MR during three main cases: mild, moderate, and severe conditions.

Methods

A 2D simplified parametric model of the mitral valve was built using Comsol Multiphysics software (Figure 1). This model was based on certain dimensions of left ventricle that was measured through an MRI image. The model included two leaflets and a semi elliptical left ventricle. Both leaflets have the same geometry and considered as symmetrical. The tips of the leaflets were set as touching in a 'normal' position [15] whereas the distance between the leaflets is 1 mm (mild MR), 3 mm (moderate MR), and 5 mm (severe MR) inspired from a physical model [18]. Blood is a virtually incompressible fluid and non-Newtonian [19-21]; however, it can be considered as Newtonian in large arteries and the heart. In the present study, we assumed blood to be a Newtonian fluid [22-23]. The leaflets were considered as isotropic and linear elastic material with Poisson's ratio of 0.33 [24] and Young's modulus of 1 MPa [25]. The viscosity of blood was set to 2.7 mPa.s and density of 1060 kg/m^3 [17]. Because the model was solved during the systolic phase, the ventricular pressure as well as the atrial pressure were considered as inputs.

Boundary conditions

The total time of systolic phase was 0.3 s which was considered for the simulation. The fluid applied a force on the leaflets leading to closure; further described elsewhere [13]. The functions of the ventricular pressure and atrial pressure were defined in the software as time-dependent inlet boundary conditions (Figure 2a, 2b) [16]. For the systolic phase, an aortic velocity function was defined at the boundary of a simplified aorta (Figure 2c, 2d). All other boundaries, including ventricle walls were considered as a non-slip condition. It should be noted that mitral leaflets and related edges were restricted from moving.

Triangular normal elements were used, with a finer meshing was set for leaflet areas in order to get more precise numerical solution (Figure 3; Table 1). A moving Arbitrary-Lagrange-Euler (ALE) mesh was applied to the leaflets and the blood flow, however, the other areas had a fixed mesh. COMSOL Multiphysics (Comsol Multiphysics, Stockholm, Sweden) was used to solve the model using a transient FSI method; described in further detail elsewhere [26-28].

Table.1: Specifications of mesh parameters

Number of vertex elements	13
Number of boundary elements	245
Number of elements	2781
Minimum element quality	0.505

Results

The preformed numerical simulation was used to predict the pressure, velocity, and Von Mises stress contours, for blood-flow and the valve leaflets, respectively, during mild, moderate, and severe MR. The extracted hemodynamic parameters are presented and compared as below.

1-Pressure:

Figure 4a-4c provides the pressure contours in three different time steps for severe MR. In severe MR, the leaflets were not attached to each other completely and there is an approximately 5 mm distance between the leaflets. The contours showed a pressure drop in the left ventricle. At a time of 0.3 s, the ventricle pressure variation was between 0.9 to 14.5 kPa with much back flow to the atrium.

Figure 5a-5c shows the pressure contours at three different time steps for moderate MR. The pressure drop within the left ventricle was lower than for severe MR but was still between 10-15 kPa. This drop was still considerable and due to a 3 mm distance between the leaflets.

Figure 6a-6c presents the pressure contours for mild MR. The ventricular pressure reached to 16 kPa which was near to that for a ‘healthy’ valve. The distance of 1 mm, between leaflets, was not effective in reducing the ventricle pressure as compared to severe MR. The backflow of blood towards the atrium was much lower than for moderate and severe MR.

Therefore, the severity of MR could be quantified from the pressure contours and decreasing of ventricle pressure. For severe MR, a decrease in ventricle pressure is predicted, down to 0.9 kPa (at 0.3 s). Furthermore, the backflow of blood was much greater toward the atrium during severe MR. Wenk et al [8] reported the left ventricle pressure between 0.8 kPa to 12.19 kPa during MR. These values are consistent with our results during moderate and severe MR, which ranged from was 0.9 kPa to 14 kPa.

2-Velocity:

The velocity streamlines of severe, moderate and mild MR are shown in Figures 7-9, respectively. Moreover, Figure 10 shows the maximum velocity at the tip of the leaflets area for three time steps during systole in three MR modes. According to these results, it can be concluded that the velocity increases up to 6 and 4.8 m/s at the leaflet tips area in severe and moderate MR, respectively, resulting to the formation of a velocity jet. However, there appeared to be a slight increase in the velocity (about 1.6 m/s) for mild condition resulting no velocity jet. The velocity changing trend is generally consistent with all MR conditions including some vortices evident in the center of ventricle. Vermenlen [29] reported the range of jet velocities between 2.6 m/s to 4 m/s during mitral valve leakage. However, Lassila [30], Thomas [31], and Grayburn [32] concluded that the jet velocity is increased to the highest value during severe MR.

3- Stress:

The stress distribution varied significantly over the leafs in our results.Stress in Severe MR case Figure 11 (a,b,c) presents the Von Mises stress distribution in severe MR case in three time steps. The stress varied between 100-500 kPa. Stress in Moderate and mild MR case Figure 12 (a,b) shows the stress distribution in moderate and mild MR case at t=0.3 s. The average of Von Mises stress on leaflets at mid systole (0.2 sec) for severe, moderate and mild MR are 275, 214 and 74 kPa, respectively. Lee et al. predicted the *in vivo* stresses of a region of interest using a numerical analysis method for the anterior leaflet of a healthy mitral valve. The total range of region of interest (ROI) stresses that they estimated were between 80.9 to 593.2 kPa, consistent with our results [33]. The stresses varied between 100 to 500 kPa over the leaflets based on our numerical results for moderate and severe MR. For instance, Wenk et al. [8] reported the effective stress in the center of the anterior leaflet to 119 kPa. Prot et al [34] results showed the leaflet stress to be 130-220 kPa. In another study, Salgo [35] reported higher stresses up to 400 kPa. The difference between the reported values comes back to different type of leaflet material models including linear isotropic, orthotropic, etc.

Discussions:

In this study, an FSI model was developed to simulate the progression of MR disease from mild to severe. Using this model, the blood hemodynamic parameters can be extracted within the progression process and compared between different intensities of MR. There are some limitations to understanding the exact physiology of MV function in healthy and diseased states due to the influence of elastic leaflets and the role of left ventricle in fluid dynamics [36-38]. Therefore, the elastic material properties were also incorporated into simulation in addition to non-Newtonian fluid properties. FSI was used because of the forces that fluid had applied on the leaflets in interaction with the structure which leads to large structural deformations.

A comparison of the results obtained between the different severities of MR has led to the following findings:

- Increasing severity of disease leads to decrease of intraventricular pressure.
- As the distance between the leaflets increases, the Von Mises stress on the leaflets increases and the return flow to the atrium increases.
- The increased velocity near the tip of the leaflets in severe MR causes the vortex in the atrium area. This vortex is due to the interaction of the back flow from the ventricle to the fluid flow in the atrium.
- Another developed vortex, inside the left ventricle, was increased during the early to the end of the systolic phase.
- It was also shown that a pair of vortices, which were developed under the leaflets, leaded to valve closure.

It was shown that this method can measure the stress patterns on the leaflets as the disease progresses. We tried to develop a model to study the hemodynamic parameters of blood flow in mitral regurgitation case. It was found that the pressure throughout the ventricle is decreased and also the velocity jet increased as the distance between leaflets is increased. Moreover, it was shown that an increase in the distance between the leaflets increases the average of Von Mises stress on leaflets at mid systole.

On the other hand, considering the same input boundary conditions for different MR states, the contraction of ventricle muscle is not effective, so the leakage plays an important role on decreasing the pressure. When the leakage occurs in one of the components, the pump will not be able to create ideal pressure. In a similar way, for severe disorder mitral function, severe leakage of blood from left ventricle to the atrium (flow back) during systole is observed and leads to decrease of the pressure in the ventricle. There are simplifications in this study, particularly around the use of a 2D model which limits assessment of mitral annular motion. In future, this may be overcome by use of a 3D model. However, in current solution times are prohibitory as regards real-time translation into clinical practice; unlike 2D models which solve over a time-frame which is compatible with clinical practice, as discussed elsewhere [39]. The model presented in this study along with the obtained results was able to capture the mitral regurgitation in different cases based on the gap size between the leaflets. It is important to consider multiple parameters for evaluating MR severity and one single measurement is not sufficient. Thus, we calculated different hemodynamic parameters of MR including pressure and velocity contours as well as leaflets' stress. These predicted results show that a regurgitant jet flow is always present in different MR cases due to an open way from left ventricle to atrium. The severity of MR was studied quantitatively as the area of the jet by above mentioned hemodynamic parameters. We believe that our model was able to demonstrate the function of MR and it can be very helpful for surgeons to use surgical plans based on predicted results of blood flow hemodynamics and leaflet stress during mitral regurgitation.

Conclusion

In this study, we have modelled the left ventricle with symmetric mitral valves integrated in 2D. In addition to the mitral valve prescribed according progression of MR disease, the FSI approach was applied to the leaflets of valves to simulate the interaction between the blood flow and elastic leaflet. We have successfully demonstrated important parameters (such as pressure and velocity) and development in the mitral regurgitation.

Compliance with Ethical Standards

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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Conflict of Interest: Authors declare that they have no conflict of interests.

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