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Development of a fluid-structure interaction model to simulate mitral valve malcoaptation

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Abstract

Mitral regurgitation (MR) is a condition in which the mitral valve does not prevent the reversal of blood flow from the left ventricle in to the left atrium. This study aimed at numerically developing a model to mimic MR and poor leaflet coaptation and also comparing the performance of a normal mitral valve to that of the MR conditions at different gap junctions of 1, 3, and 5 mm between the anterior and posterior leaflets. The results revealed no blood-flow to the left ventricle when a gap between the leaflets was 0 mm. However, MR increased this blood-flow with increases in the velocity and pressure within the atrium. The pressure within the aorta did not vary meaningfully though (ranging from 22 kPa for a 'healthy' model to 25 kPa for severe MRD). The findings from this study have implications not only for understanding the changes in pressure and velocity as a result of the MR in the ventricle, atrium, or aorta, but also for the development of a computational model suitable for clinical translation when diagnosing and determining treatment for MR.

Keywords: blood flow; fluid-structure interaction; left atrium; left ventricle; Mitral regurgitation.

Introduction

Mitral regurgitation (MR) is a condition in which the leaflets of the mitral valve do not prevent backflow of the blood from the left ventricle to the left atrium **[1],[2],[3]**. This is often due to poor closure, or coaptation, between its leaflets; known as mal-coaptation. Thus, if MR is severe, the pressure of the left atrium increases leading to symptoms such as dyspnea, fatigue, orthopnea, and pulmonary edema **[4]**. Although annular dilation, and its subsequent effect on coaptation, has been assessed *in vitro* **[5]**, there is limited understanding of the effect of the specific mode of mal-coaptation on the subsequent hemodynamic characteristics of the blood flow during MR between the left atrium, left ventricle, and the aorta. MR can be studied clinically, but it does not offer the possibility to assess variables associated with mal-coaptation independently to assess how they contribute to subsequent hemodynamics during MR. Computational modelling, and in particular, transient Fluid-Structure Interaction (FSI) **[6]** offers the potential to determine the mechanisms linking altered mechanics and coaptation between mitral valve leaflets, with the resulting pathophysiological hemodynamics.

There is an extensive range of computational modelling of the mitral valve within the literature. For instance, Wenk *et al*. **[7]** proposed a finite element (FE) model for the left ventricle with MR using magnetic resonance imaging (MRI) data from sheep. Stevanella *et al*. **[8]** presented a patient-specific structural FE model of the mitral valve to assess mitral annuloplasty procedures. A three-dimensional FE model of the mitral valve has also proposed to assess the nonlinear mechanical performance of the anterior and posterior leaflets during the diastole and systole **[9]**. Surgical repair of the mitral valve has been assessed too **[10],** along with the effect of collagen concentration within the mitral valve leaflets **[11]**. More recently, there has been a focus on combining Computational Fluid Dynamics (CFD) with end-diastolic geometry and time-dependent

deformation of the left ventricle cavity **[12]**, as well as MR flow **[13]**. CFD has also been used to assess insufficiency through the mitral valve Sonntag *et al*. **[14]**. However, regardless of the depth of literature, currently no such studies have determined a mechanical pathway which links the specific pathophysiological hemodynamic characteristics during MR to the altered leaflet mechanics which result in mal-coaptation. Even an initial step of assessing the influence of a gap between the two mitral leaflets has not been assessed; despite the clinical importance of such studies, and their potential to be used to propose novel repair strategies, both the computational and experimental literature is very much limited **[15]**.

This study was aimed at developing a transient FSI model of the mitral valve able to predict mal-coaptation. The model geometry is based on subject-specific MRI data. For this initial development, a two-dimensional (2D) model has been used. While three-dimensional models are of value [16], the timescales associated with solving 2D models at present more closely match clinical timeframes [17]. This initial model has focused on hemodynamic assessment of blood flow through the left atrium, left ventricle, and the aorta, during mal-coaptation of the anterior and posterior mitral valve leaflets due to gap sizes of 1, 3, and 5 mm.

Materials and methods

An MRI scan (Siemens, Germany,1.5 Tesla) of a mitral valve was obtained from a 60-year-old male. Ethical approval was obtained from Tehran Modarres Hospital. The mitral valve scanned had normal coaptation. From this scan, distinct MR cases were simulated using a 2D model (**Fig. 1**).

Four cases were simulated. The first model included tightly coapting anterior and posterior leaflets so that no MR occurred across the mitral valve (Case A). The second model included a 1 mm gap

between the leaflets, and was considered as a mild MR model (Case B). The third model included a 3 mm gap between the leaflets, representing fully developed MR (Case C). The last model included a 5 mm gap, simulating severe MR (Case D). Left atrial and ventricular systolic pressures were applied as boundary conditions **[18],[19]** where the blood velocity (flow rate if considered over the cross-sectional area of the aorta) was applied as a further boundary condition **[20]**. As the mitral valve is closed during systole, the leaflets were assumed to be fixed in position. This boundary condition would mimic the mitral valve leaflets following the initial elongation of chordae tendineae; consistent with previous studies **[21]**.

Blood flow was assumed to be laminar, incompressible, and Newtonian; a suitable approximation under large-scale flow as occurs within the heart **[22]**. The viscosity of blood was taken to be 5.5 mPa/s with density of 1056 kg/m^3 **[23], [24]**. Anterior and posterior mitral leaflets were assumed to behave as linear elastic materials (with a Young's modulus of 1 and 2 MPa, respectively). The density and Poisson's ratio of the leaflets applied to the model were 1060 kg/m^3 and 0.488, respectively **[25], [26]**.

Triangular elements were used to generate the mesh. The mesh density analyses have been conducted to select the appropriate mesh size (stress was assessed with mesh density). The number of elements used in the model was 3309. The simulation time was set to run for 0.45 s, i.e. only systole was modelled **[27]**.

FSI was used to perform transient, and simultaneous simulations of the mitral valve. Simulations were performed using Comsol Multiphysics (Comsol Multiphysics, Stockholm, Sweden). The formulation employed led to the following physical restraints/coupling to enable interaction between simulation of fluid flow and structural deformation: a) the deformation of the contact points of the fluid (blood) and solid (Leaflet) were coupled (i.e. rate of change of solid

boundary displacement is matched by the velocity of blood); b) the planar force of the fluid in the contact point of the fluid and solid acts as the planar force of the solid (i.e. the loading condition applied to the leaflets); and c) a no slip condition is applied to the fluid boundary **[28]**.

Results

Velocity contours at 0.2 s (during systole) are provided **Fig. 2** for all four cases. For the 'healthy' model (Case A), MR was not possible **[29]** and a vortex ensued behind the leaflets. When MR was simulated (Cases B-D), the blood volume and the velocity increased due to an increasing gap between the leaflets. The result is blood-flow into the atrium (**Fig. 2**). For mild MR (Case B), the leakage rate was low (around 2.5 m/s). However, blood-flow velocity reached 5 m/s for Cases C and D. For severe MR (Case D), the velocity was such that a large vortex ensued within the left ventricular cavity.

The velocity of blood within the left atrium is provided in **Fig. 3**. For Case A, this velocity was zero. For MR, blood flow increased to peak values of 0.81, 1.63, and 2.42 m/s for Cases B, C, and D, respectively. This trend continued from the time at which these peaks occurred up to the end of the simulation.

The time-dependency of left atrial blood pressure is provided in **Fig. 4**. For Case A, these pressures were in agreement with experimental data **[30]**. For Case B, similar trends were predicted for time-dependent pressures, but a small alteration in the maximum (0.3 Kpa) and minimum (1.9 Kpa) pressures did occur. However, for Cases C and D, an abnormal pressure trend was predicted. This abnormal pressure was related to the rate of systolic ventriculo-atrial blood-flow; in essence, the velocity of MR. Peak pressures for Cases C and D were 2.12 and 2.90 kPa, respectively.

Time-dependent ventricular pressure adjacent to the mitral valve is provided in **Fig. 5**. There is an increased pressure during early systole (to 5 kPa) for both cases C and D. For Case D this pressure peaked at 7.80 kPa. The graphs predicted that the increased size of the gap, C and D cases, led to a ventricular pressure increase of 5 to 7 kPa comparing to normal situation, Case A.

This model has made predictions of altered MR hemodynamics and a potential relationship to left atrial pressure – this might have implications for LV and LA remodeling. Also, there may be some comparisons to literature (e.g. clinical / experimental).

Time-dependent aortic pressure is displayed in **Fig 6**. No meaningful differences in pressure were predicted for aortic blood-flow. These values ranged from peak pressures 22 kPa for a 'healthy' model (Case A) to 25 kPa for severe MR (Case D. Fig 7 represents the pressure contours at 0.2 s (during systole) for all cases.

Discussions

We have presented a model which has made predictions of altered MR hemodynamics and a potential relationship to left atrial pressure. This might have implications for left ventricle and left atrium remodeling. Comparison of four MR models showed different hemodynamic characteristics based on the size of the gap between leaflets. The blood jet generated small vortexes in mild and severe MRs.

Looking to the pressure contours, we found out that the absence of mitral regurgitation in model-A leads to an increase of systolic pressure in the left ventricle. The results is in agreement with Lassila et al [31] findings. On the other hand, Thomas et al [32] showed that peak ejection velocity was seen to increase due to MR severity. This is also in agreement with our findings.

During the ventricular systolic phase the left ventricle contradiction, the rate of blood flow from the mitral is very low or zero [33]. The leaflet close mechanism depends on the distance of ring

vortexes of each ventricle during systole [34]. These vortexes could not be modeled in the commercial FE software. Therefore, the leaflets were considered as fixed components. This assumption allowed the mitral valve was closed during systole and the blood flow showed no effect on the leaflets. The limitation of this study was that we considered a fixed left ventricle wall which could not mimic the ventricle failing to reproduce the necessary pressures during severe MR.

We believe that this is the first model which assesses mal-coaptation and its relationship with MR: increasing MR velocity, left atrium pressure and other hemodynamic parameters. We also hypothesize that the reduced aortic flow may not be due directly to MR but to increased difficulty of the heart to pump blood. Although the obtained results were clinically shown but our work is the first to link actual changes in coaptation to specific hemodynamic factors including pressure and velocity. The success of this study opened the way for further development in to a clinical tool. On the other hand, there were several limitations in our study which should be considered for further studies. The inclusion of myocardium as well as endocardium and the influence of these structures should be investigated therefore another fluid structure interaction model is required to show these structures responses and the flow inside the left ventricle. Dynamic motion of leaflets should also evaluated. It is also suggested to make more accurate anatomically model using three dimensional echocardiography or new MRI sets.

Conclusions

An FSI model of the left side of the heart has been produced, from an MRI scan to study mitral valve mal-coaptation. Increased mal-coaptation resulted in increased left atrial pressure, which would presumably lead to enlargement (as seen clinically). A bigger gap between the leaflets led

to a large vortex within the left ventricle and higher blood velocity in the atrium. The pressure adjacent to the mitral valve also increased with increased mal-coaptation. These findings have implications not only for understanding alterations in pressure and velocity as a result of the MR in the ventricle, atrium, or aorta, but also for providing a comprehensive numerical model suitable for clinical translation. We believe that this model, along with improved version, is a powerful tool for future clinical scenarios as it could capture the presence of MR. However, the model should be improved in number of ways as mentioned before.

Compliance with Ethical Standards

Funding: None.

Conflict of Interest: None.

Ethical approval: Ethical approval was provided under the permission of Modarres Hospital, Tehran, Iran.

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