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Patient-specific CT-based 3D Passive FSI model for left ventricle in hypertrophic obstructive cardiomyopathy

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Abstract

Left ventricular outflow tract obstruction is observed in 70% of patients with hypertrophic cardiomyopathy, which occurs in about 1 of every 500 adults in the general population. It has been widely believed that the motion of the mitral valve, in particular, its systolic anterior motion (SAM), attributes significantly to such obstruction. For a better understanding of the mitral valve motion, a 3D patient-specific fluid-structure interaction model of the left ventricle from a patient with hypertrophic obstructive cardiomyopathy based on computed tomography (CT) scan images was proposed in this study. The entire 3D left ventricle, including the mitral valve, was reconstructed from contrast enhanced CT images and the computational analysis was performed in ADINA. Displacement, structural stress, pressure, flow velocity and shear stress within the left ventricle and mitral valve were extracted to characterize their behavior. The maximum shear stress on mitral valve was 9.68 dyn/cm². It was found that the pressure on its posterior leaflet was higher than that on the anterior leaflet and the peak pressure on the mitral valve was 93.5 mmHg which occurred at pre-SAM time. High angles of attack ($54.3 \pm 22.4^\circ$) were found in this patient. The methodology established in this study may have the potential to clarify the mechanisms of SAM

and ultimately optimize surgical planning by comparing the mechanical results obtained from preoperative and postoperative models.

Keywords

Left ventricle; hypertrophic obstructive cardiomyopathy; systolic anterior motion; fluid-structure interactions

Introduction

Hypertrophic cardiomyopathy occurs in about 1 of every 500 adults in the general population (Semsarian et al. 2015). The thickening of interventricular septum can cause left ventricular outflow tract obstruction (LVOTO), which is present in approximately two-thirds of patients with hypertrophic cardiomyopathy, thus constituting a diagnosis of hypertrophic obstructive cardiomyopathy (HOCM). Patients with HOCM may suffer from symptoms including chest pain, dyspnea, and syncope. Some patients are at increased risk of heart failure and sudden cardiac death. For patients with intractable symptoms to drug therapy, septal myectomy (Morrow procedure) is the routine clinical surgery (Maron and Maron 2015, McCully et al. 1996). Surgical septal myectomy can eliminate systolic anterior motion (SAM) of the mitral valve, which is the dominant reason for dynamic obstruction, thus relieving LVOTO.

However, surgical myectomy is challenging as the extent of myectomy is hard to determine (Kim et al. 2016, Maron et al. 2015). Inadequate excision cannot abolish SAM to restore the normal hemodynamic function, while excessive myectomy may produce complete heart block or ventricular septal defect. Therefore, a non-invasive method that enables an optimal surgery plan is urgently needed. As the first step towards to this aim, it is essential to characterize the SAM of the mitral valve as the abnormal hydrodynamic forces were proposed to be responsible for this disease (Jiang et al. 1987, Sherrid et al. 1993, Sherrid et al. 2000). Computational modeling and medical imaging technologies have made considerable advances in biological and clinical research in recent years (Axel 2002, Costa et al. 1999, Domenichini and Pedrizzetti 2015, Guccione et al. 1993, Humphrey 2002, Hunter et al. 2003, Kerckhoffs et al. 2007, McCulloch et al. 1992, Nash MP 2000, Peskin 1975, Peskin 1977, Peskin 1989, Saber et al. 2001, Tang et al. 2008, Tang et al. 2010, Tang et al. 2011, Vetter and McCulloch 1998, Vetter and McCulloch 2000). Use of computer-assisted procedures is becoming more and more popular in the clinical decision making process and computer-aided surgeries. Peskin pioneered heart modeling with his celebrated immersed boundary method designed to study blood flow features in an idealized geometry with FSI (Peskin 1975, Peskin 1977, Peskin 1989). More recent efforts, including the MRI-based fluid or structure only model, and the fluid-structure interaction model, were developed to investigate some basic flow and stress/strain behaviors (Axel 2002, Costa, Takayama, McCulloch and Covell 1999, Guccione, Waldman and McCulloch 1993, Humphrey 2002, Hunter, Pullan and Smaill 2003, Kerckhoffs, Neal, Gu, Bassingthwaite, Omens and McCulloch 2007, McCulloch, Waldman, Rogers and Guccione 1992, Nash MP 2000, Saber, Gosman, Wood, Kilner, Charrier and Firmin 2001, Tang, Yang, Geva and Del

Nido 2008, Tang, Yang, Geva and Del Nido 2010, Tang, Yang, Geva, Gaudette and Del Nido 2011, Vetter and McCulloch 1998, Vetter and McCulloch 2000). However, in these studies, the mitral valve was usually excluded due to the difficulties in acquiring accurate data of a person's mitral valve and its big deformation, solid-solid and solid-fluid interaction during a cardiac cycle. As an asymmetric bileaflet, the mitral valve is located at the inflow tract of the left ventricle. It has been shown that incorporation of the mitral valve into the numerical model will give more realistic flow pattern predictions in ventricle (Domenichini and Pedrizzetti 2015, Seo 2014), in particular in the case when the abnormal hydrodynamic phenomena caused SAM is investigated. However, comprehensive analysis considering both the left ventricle and the mitral valve, and the interaction between them and blood, is still lacking. In this study, a patient-specific computed-tomography (CT) based 3D fluid-structure interactions (FSI) model for the left ventricle of an HOCM patient was reconstructed to investigate the intraventricular flow and structure stress/strain distributions.

Methods

Data acquisition

A 54-year-old male with HOCM scheduled for surgical septal myectomy was recruited in this study. The investigation was approved by the review board on human subject research (Fuwai Hospital, Chinese Academy of Medical Sciences), and informed consent was obtained. Pre-operative ECG-gated echocardiography showed a left ventricular outflow gradient of 81 mmHg and severe SAM of the mitral valve. SAM began from 8% inter beat (RR) interval in the cardiac cycle. Color Doppler imaging of blood flow and cardiac tissue were obtained. ECG-gated cardiac CT scans were performed, which covered every 5% RR interval in the cardiac cycle. To investigate the mechanisms of initiation for the SAM, CT images of the patient's left ventricle at pre-SAM time point (5% RR interval) were selected to construct the geometry model. There were a total of 130 slices (slice thickness 0.625 mm) covering the left ventricle, and one slice out of every 4 slices (44 slices in total) were used to construct the 3D FSI model. Figure 1. presents 4 selected CT image slices, segmented contour plots of the left ventricle, the mitral valve, and the aorta for the left ventricle modeling construction. Figure 2. gives the stacked CT contours and left ventricle inner/outer surface plots showing the mitral valve and the aorta. Patient-specific systolic (110 mmHg) and diastolic (70 mmHg) pressure conditions from the last hospital admission were used in the simulation. The left ventricle volumes at the end of diastole and systole were obtained by cardiac magnetic resonance imaging.

Solid Model

The material property of the left ventricle was assumed to be hyperelastic, isotropic, incompressible and homogeneous. The governing equation (summation convention is used) for the structure is as follows,

$$\rho v_{i,tt} = \sigma_{ij,j}, i, j = 1, 2, 3 \quad (1)$$

Where ρ is the density of the ventricle muscle, t stands for time, i and j label spatial coordinates, v is the displacement vector, σ is the stress tensor, $f_{.,j}$ stands for derivative with respect to the j^{th} variable. The strain-displacement relations is given by,

$$\varepsilon_{ij} = (v_{i,j} + v_{j,i} + v_{\alpha,i}v_{\alpha,j})/2, i, j, \alpha = 1, 2, 3 \quad (2)$$

where $\varepsilon = [\varepsilon_{ij}]$ is the Green-Lagrange strain tensor. The modified non-linear Mooney-Rivlin strain energy density was used to describe the material properties with constants chosen to match available experimental data (Humphrey 2002, K.J. 2002, Yang et al. 2007),

$$W = c_1(I_1 - 3) + c_2(I_2 - 3) + D_1[e^{D_2(I_1 - 3)} - 1] \quad (3)$$

where $I_1 = \Sigma C_{ii}$, and $I_2 = \frac{1}{2}(I_1^2 - C_{ij}C_{ij})$ are the first and second strain invariants, $C = [C_{ij}] = X^T X$ is the right Cauchy-Green deformation tensor, $X = [X_{ij}] = [\partial x_i / \partial a_j]$, where x_i is the current position, a_i is the original position, and c_i and D_i are material constants: $c_1 = 12.88$ kPa, $c_2 = 0$, $D_1 = 5.04$ kPa, and $D_2 = 2$.

Fluid Model

Blood flow in the left ventricle was assumed to be laminar, Newtonian, viscous and incompressible. The Navier-Stokes equation with Arbitrary Lagrangian Eulerian formula was used as the governing equation. To simplify the computational model, the cardiac cycle was split into two phases as follows, 1) the filling phase, when blood flows into the left ventricle through the mitral valve and the outlet was closed; 2) The ejection phase, when blood was ejected out of the left ventricle, the outlet (aortic valve) kept open and the inlet (mitral valve) was closed. When the inlet or outlet was closed, flow velocity was set to zero and pressure was left unspecified. The pressure condition scaled was based on systolic and diastolic blood pressure conditions from last hospital admission and the pressure difference (between the left ventricle and the aorta) obtained from ultrasound scanning.

Since the left ventricle muscle was treated as passive material, pressure conditions were modified so that the left ventricle could be inflated properly by fluid forces. No-slip boundary conditions and natural force boundary conditions were specified at all interfaces to couple fluid and structure models together (K.J. 2002, Tang, Yang, Geva and Del Nido 2008). Putting these together, we have

$$\rho(\partial \mathbf{u} / \partial t + ((\mathbf{u} - \mathbf{u}_g) \cdot \nabla) \mathbf{u}) = \nabla p + \mu \nabla^2 \mathbf{u} \quad (4)$$

$$\nabla \cdot \mathbf{u} = 0 \quad (5)$$

$$\mathbf{u}|_F = \partial \mathbf{x} / \partial t \quad (6)$$

$$p|_{\text{valve}} = p_{in}(t), \mathbf{u}|_{\text{aorta}} = \mathbf{0}(\text{filling phase}) \quad (7)$$

$$p|_{\text{aorta}} = p_{out}(t), \mathbf{u}|_{\text{valve}} = \mathbf{0}(\text{ejection phase}) \quad (8)$$

$$\sigma_{ij}^f n_j^f|_{\text{interface}} = \sigma_{ij}^s n_j^s|_{\text{interface}} \quad (9)$$

where $\mathbf{u}$ and p are fluid velocity and pressure, $\mathbf{u}_g$ is mesh velocity, F stands for the left ventricle inner wall, σ is structure stress tensor, (superscripts, f and s , indicate blood and the left ventricle, respectively), and $\mathbf{n}$ is the outward normal directions. Together with equation (1)–(3), we completed the FSI model.

Pre-Shrink process, mesh generation and solution method

Under the *in vivo* condition, the ventricles were pressurized and the zero-stress ventricular geometries were not known. In our model construction process, a pre-shrink process was applied to obtain the starting geometry (the zero-load geometry) for the computational simulation. The initial shrinkage rate was 5% and end-systolic pressure was applied so that the ventricles would regain its *in vivo* morphology (Tang, Yang, Geva, Gaudette and Del Nido 2011).

Volume component-fitting method was employed to generate meshes for left ventricle with irregular geometry (Tang, Yang, Geva and Del Nido 2008, Yang, Tang, Haber, Geva and Del Nido 2007). Using this technique, both the left ventricle and fluid domains were divided into thousands of small “volumes” to curve-fit the geometry. The edge of each volume will be further divided into several divisions to generate the final mesh in ADINA (ADINA R&D, Watertown, MA) (Fig. 3). By applying this method, the mesh generated would not be too distorted under large deformation. Mesh analysis was performed by decreasing mesh size by 10% until solution difference was less than 2%. The mesh was then chosen for our simulation. The fully coupled FSI model was solved by ADINA using unstructured finite elements and the Newton-Raphson iteration method (K.J. 2002, Tang et al. 2016, Tang, Yang, Geva and Del Nido 2008, Yang, Tang, Haber, Geva and Del Nido 2007).

Angle of attack onto the leaflet

As suggested previously, the septal bulge redirects the blood flow towards a posterior to anterior direction, and the left ventricular ejection flow is thought to anteriorly push the mitral leaflet causing SAM (Nakatani et al. 1996, Ro et al. 2014, Sherrid, Chu, Delia,

Mogtader and Dwyer 1993, Sherrid, Gunsburg, Moldenhauer and Pearle 2000). To assess the effect of this drag force, the angle of attack onto the posterior surface of the protruding mitral valve leaflets at pre-SAM time point was investigated. At each slice, a vector (V_1) was drawn through the point of coaptation closest to the annulus and bisects the angle of posterior leaflet and anterior leaflet (Nakatani, Schwammenthal, Lever, Levine, Lytle and Thomas 1996). Vector V_2 was the velocity vector at selected flow point which was just upstream from the tip of the posterior mitral leaflet. The following formula was used to calculate the angle between V_1 and V_2 ,

$$\text{Angle} = \arccos\left(\frac{V_1 \cdot V_2}{\|V_1\| \|V_2\|}\right) \quad (10)$$

We selected three flow points on each slice, and the mean value of the angles between V_1 and the velocity at these three points was then used to indicate the angle of attack at this slice. The technique was similar to a previous study (Ro, Halpern, Sahn, Homel, Arabadjian, Lopresto and Sherrid 2014). Figure. 4. presents the vector flow map for slice 7 showing selected points.

Results

A completed cardiac cycle simulation included: 1) the inlet pressure increased, blood filled into the left ventricle through the mitral valve and its volume increased; 2) when switched to the ejection phase, the mitral valve closed and the aortic valve (outlet) opened up, and blood got ejected out and the left ventricle volume decreased. The obtained simulation results for the left ventricle volume and maximum velocity on valve during two cycles were presented in Fig. 5. At pre-SAM point (5% RR interval), the obtained predicted left ventricle volume was 106.5 cm^3 , which matched well with CMR measurement (106 cm^3). The simulation results (including velocity, displacement, and stress) at pre-SAM time point of the second cycle were selected to characterize the material behavior of the ventricle and valve.

Figure. 6. a) gives the position of a cutting surface chosen to present the simulation results. At pre-SAM time point, the maximum velocity on the cutting surface was 32.08 cm/s ; the maximum displacement was 0.5 cm . It can be seen from Fig. 6 d) that large displacement was observed in the regions with papillary muscles. Figure. 7. presents the band plots of shear stress and pressure distribution on the mitral valve. The pressure on the posterior leaflet of the mitral valve was higher than that on the anterior leaflet, although the difference of the pressure between anterior and posterior leaflet was not significant. The shear stress was higher on the anterior leaflet than that on the posterior leaflet. The maximum value of shear stress was 9.68 dyn/cm^2 (Fig. 7). Table 1 lists the angles of attack of velocity vector flow onto the posterior surface of the mitral valve for each slice. The maximum value of the angle is 84.9° and the average value is $54.3 \pm 22.4^\circ$ and the angles of attack for 6 out of 14 slices were greater than 60° .

Discussion

To our best knowledge, this study was the first attempt to perform a CT image-based patient-specific FSI analysis with the consideration of the left ventricle and the mitral valve in a HOCM patient. Compared to CMR images, CT images have a better resolution. The slice thickness for CMR is 6–8 mm. However, the slice thickness of CT images is only 0.625 mm, which is about 1/10 of CMR. It's possible to obtain the morphology of the mitral valve based on CT images. The stress/strain distribution on MV and more realistic intraventricular flow pattern predictions in LV were provided in this study.

SAM of the mitral valve is the dominant reason for dynamic LVOTO in HOCM. Its occurrence is closely related to the hemodynamics in the left ventricle, as heart rate, volume, blood pressure and myocardial contractility can all influence the initialization and extent of SAM (Ibrahim et al. 2012). The hydrodynamic mechanism of SAM remains unclear. The Venturi effect was initially thought to be responsible for the occurrence of SAM (E 1997, EJ 1998, Schlant RC 1994). However, several studies have proved that SAM began very early in the systole, when the left ventricular outflow tract velocity was low (Ro, Halpern, Sahn, Homel, Arabadjian, Lopresto and Sherrid 2014, Sherrid, Gunsburg, Moldenhauer and Pearle 2000), and thus precluding the existence of the Venturi effect at that moment. Flow drag, the pushing force of flow, has been considered as the dominant hydrodynamic force that initiates SAM (Jiang, Levine, King and Weyman 1987, Nakatani, Schwammenthal, Lever, Levine, Lytle and Thomas 1996, Ro, Halpern, Sahn, Homel, Arabadjian, Lopresto and Sherrid 2014, Sherrid, Chu, Delia, Mogtader and Dwyer 1993, Sherrid, Gunsburg, Moldenhauer and Pearle 2000). In a previous study by Ro et al. (Ro, Halpern, Sahn, Homel, Arabadjian, Lopresto and Sherrid 2014), vector flow mapping based on 2D Doppler imaging was performed to show the spatial relationship of the left ventricular flow and the mitral valve leaflet. They found that the septal bulge redirected the blood flow towards a posterior to anterior direction, thus increasing the angle of attack ($>60^\circ$) onto the posterior surface of the protruding mitral valve, which was then pushed anteriorly towards the septum. The high angles of attack ($54.3 \pm 22.4^\circ$) were also found in this research. Moreover, our method may provide more comprehensive information since it enabled us to obtain the global 3-dimensional flow vector field and quantify the mechanical stress on the mitral valve, while the latter directly induced SAM.

Several improvements can be added to our models: a) Valve opening. While the exact valve opening was not included in the current model, therefore, the flow in diastole period might be slightly different to the real one, yet the fluid flow in diastole period is not important for the mechanisms of SAM; b) Fiber orientation and anisotropic models. The single and multi-layer anisotropic models could be introduced to seek possible improvement in computational prediction accuracies. However, the irregular, disorganized alignment of muscle cells or myocardial disarray was found normally in the heart in HCM patients. The fiber orientation data was not able to be obtained with current technology; c) Active contraction behavior. While the mechanism driving the left ventricle motion in our model is different from the real heart, our passive model can still simulate the left ventricle motion, deformation, and fluid flow to match measured patient-specific data with proper pressure conditions. Actually, it is very difficult to determine the active stresses/strains with current technology. To add active

contraction into our model, one way is to introduce an external force field. However, measurement and validation of an external force field was currently not possible. Another way to introduce the contraction is to make the left ventricle material stiffer during systole. Time-dependent material stiffness may be applied to model left ventricle contraction. The time-dependent material parameters can be numerically determined by matching the left ventricle volume-pressure data. This will be a possible future improvement of our model. It should be noted that this will lead to increasing the complexity and computational cost of the model significantly.

The proposed patient-specific CT-based computation model with fluid-structure interactions for the left ventricle will be used to illustrate the mechanisms of SAM and ultimately optimize surgical planning. SAM will be abolished by successful surgery, and a post-operation model will be constructed after receiving the post-operation data. The obtained results of the flow field and mechanical stress on the mitral valve by solving the post-operation model will be compared with preoperative counterparts, and thus might clarify the mechanisms of SAM. This model can also be used in virtual surgical planning. Upon receiving the preoperative data, a region in the hypertrophic septum can be selected to be “resected” in our proposed patient-specific computational model. The altered mechanical stress distributions on the mitral valve and fluid flow pattern will be numerically obtained and analyzed to predict if the “resection” is sufficient to eliminate SAM. The region will be numerically adjusted for optimal surgical planning. The post-surgery data will be used as the gold standard for validation of the computational assessment and predictions. These applications need to be established based on large scale comparative patients’ studies and follow-up observations.

Conclusion

A CT image based patient-specific left ventricle model for HOCM patient was proposed to obtain the blood flow pattern and stress/strain distributions at pre-SAM time point. Our preliminary results indicated that the obtained predicted volume was well matched with CMR volume data and the angles of attack of velocity vector flow were high. The band plots of shear stress, Stress- P_1 , and pressure distribution on the mitral valve were obtained, which could help for illustrating the mechanisms of SAM. The model proposed in this study may have the potential to be used in patient-specific surgical planning for HOCM patients. Large scale comparative patients’ studies are needed to better interpret the computational results and validate the computational predictions for the surgical outcomes.

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Nomenclature

CT   computed- tomography

FSI	fluid-structure interactions
HCM	Hypertrophic cardiomyopathy
HOCM	hypertrophic obstructive cardiomyopathy
LVOTO	Left ventricular outflow tract obstruction (LVOTO)
SAM	systolic anterior motion

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Figure 1.

Selected CT images (beginning of systole) were acquired from a hypertrophic obstructive cardiomyopathy (HOCM) patient. a) Selected CT images from a patient with HOCM; b) Segmented contours of the left ventricle, the mitral valve, and the aorta corresponding to CT images shown in a).

a) Re-constructed 3D Geometry
of LV from CT Images;

b) Inner surface of
LV with MV

Figure 2.
Reconstructed 3D geometry of the left ventricle showing the mitral valve and the aorta.

a) 3D Finite Element Mesh for Solid Model of LV

b) 3D Finite Element Mesh for Fluid model of LV

Figure 3.
3D Finite Element Mesh for Solid/Fluid model of the left ventricle showing valve positions.

Figure 4.

Vector flow map for slice 7 showing three flow points (p_1, p_2, p_3) selected to determine the angle of attack onto the posterior leaflet.

Figure 5.
Computational results for LV volume and velocity.

a) Shading image showing the cutting surface   b) Velocity vector plot on cutting surface

c) Stress- P_1 on cutting surface

d) Displacement on cutting surface

Figure 6.

Band plots of velocity vector, stress- P_1 , and displacement on a cutting surface at the pre-SAM time point: a) the position of the cutting surface; b) velocity vector plot on cutting surface; c) stress- P_1 ; d) displacement.

Figure 7.
Band plots of shear stress and pressure distribution on the mitral valve.

Table 1.

Summary of the angles of attack of velocity vector flow onto the posterior surface of the mitral valve leaflet for each slice.

Slice #	Angle	Slice #	Angle
1	77.8	8	37.5
2	66.7	9	39.0
3	61.4	10	49.9
4	84.9	11	56.3
5	75.2	12	65.9
6	40.8	13	38.7
7	37.5	14	3.6