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Numerical simulation study on systolic anterior motion of the mitral valve in hypertrophic obstructive cardiomyopathy

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ABSTRACT

Background: The hydrodynamic mechanisms of systolic anterior motion (SAM) of the mitral valve in hypertrophic obstructive cardiomyopathy (HOCM) remain unclear.
Methods: Based on computed tomography (CT) images and clinical data, pre- and post-operative computational models of the left ventricle were constructed for 6 HOCM patients receiving septal myectomy. SAM was abolished in 5 patients and persisted in one after septal myectomy surgery. The obtained simulation results including flow field of the left ventricle and mechanical behaviors of the mitral valve (MV) between pre- and post-operative FSI models were compared.
Results: The pressure difference and shear stress on the mitral valve leaflets (MVL) were relatively high pre-operatively, and decreased significantly after satisfactory surgery, but remained high following failed surgery. The significant increase in coaptation-to-septal distance was found when SAM was abolished.
Conclusions: Our results indicated that high pressure difference and shear stress on the MVL might directly initiate SAM in HOCM. Successful septal myectomy enlarged the coaptation-to-septal distance sufficiently to keep the MVL away from the ejection flow, thereby eliminating SAM.

1. Introduction

Systolic anterior motion (SAM) of the mitral valve (MV) is the dominant cause of left ventricular outflow tract (LVOT) obstruction in hypertrophic obstructive cardiomyopathy (HOCM). Anatomical factors, including hypertrophic basal septum, elongation of mitral valve leaflets (MVL), anterior displacement of papillary muscles and anomalous muscle bundles, have been confirmed to contribute to SAM [1–8]. Among these pathological changes, hypertrophic septum acts as the most decisive factor, providing the basis for septal myectomy to eliminate SAM. However, the mechanical mechanisms of SAM remain unclear. The Venturi effect was initially considered responsible for the occurrence of SAM [9,10]. However, several studies have proved that SAM began very early in the systole, when left ventricular outflow tract (LVOT) velocity was low [11], thus precluding the existence of the Venturi effect at that moment. Flow drag, the pushing force of flow, has been widely accepted as the dominant hydrodynamic force that initiates SAM [12–14]. It is assumed that the septal bulge redirects the blood flow towards a posterior to anterior direction, thus increasing the angle of attack onto the posterior surface of the protruding MVL, which is then pushed anteriorly towards the septum [15]. However, although the altered flow field has been detected by vector flow mapping (VFM) recently [15], its mechanical effect on the structure of the MVL remains unavailable.

Numerical simulation approach is a novel method to investigate the hemodynamic status and structural behaviors in the heart [16,17]. In brief, the principle of the numerical simulation is to construct a three-dimensional computational model for the heart based on patient-specific data (including imaging data and measured hemodynamic parameters), and to use numerical methods to obtain the results of intraventricular flow and stress/strain distribution for the structure.

Abbreviations: CT, computed tomography; ECG, electrocardiography; FSI, fluid–structure interaction; HOCM, hypertrophic obstructive cardiomyopathy; LV, left ventricle; LVOT, left ventricular outflow tract; LVOTG, left ventricular outflow tract gradient; MV, mitral valve; MVL, mitral valve leaflets; SAM, systolic anterior motion; VFM, vector flow mapping.

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In this study, a patient-specific computed-tomography (CT) based 3D fluid–structure interactions (FSI) analysis was applied to simulate the active contraction of the left ventricle (LV) and the intraventricular flow in LV, and to assess the interactions between blood flow and the MVL for HOCM patients. To the best of our knowledge, this study was the first attempt to construct patient-specific active-contraction LV fluid–structure interaction (FSI) models with MV incorporated in HOCM patients based on CT images. The hemodynamic statuses and structural behaviors with and without SAM (after septal myectomy) at a pre-SAM time point were compared to investigate the mechanisms of SAM.

2. Methods

2.1. Patients selection and characteristics

Between April 2016 and April 2017, 6 patients (5 male, average age 47 yrs) with HOCM receiving septal myectomy at our institution were recruited in this study. All patients had severe SAM with septal thickness >20 mm, and all of them were in sinus rhythm. Patients were excluded if they had mid-LV obstruction, latent obstruction, intrinsic MV diseases, bulky anomalous muscle bundles, systolic dysfunction or other combined intracardiac malformations. The Institutional Review Board of Fuwai Hospital approved the protocol, and written informed consent was obtained from all patients involved. The operation techniques had been described previously [18], and no concomitant MV procedures (repair or replacement) were performed in these patients. Echocardiographic characteristics before and after surgery are shown in Supplemental Table 1. These patients were divided into two groups, with Group 1 including Patient Nos. 1–5 with satisfactory surgery outcomes, and Group 2 including Patient No. 6 with unsatisfactory surgery outcome. In Group 1, SAM and mitral regurgitation were successfully eliminated, and the LVOTG decreased significantly as well; in contrast, in Group 2, SAM and mitral regurgitation persisted after surgery, and the LVOTG remained still high.

2.2. Data acquisition

ECG-gated cardiac CT scans were performed at every 5% RR interval in the cardiac cycle. To investigate the mechanisms of the initiation of SAM, CT images of patients' LV at the pre-SAM time point (5% RR interval) were selected to construct the geometry model, since the beginning time of SAM ranged from 5% to 8% RR interval in the cardiac cycle in all these 6 patients. The field of view of the CT images was 256 mm × 256 mm, and the matrix size was 512 × 512. The original slice thickness of the CT images was 0.625 mm, and there were about 110–150 slices of images covering the LV. To facilitate the modeling construction process, one from every 4 slices was used to construct the 3D FSI model. The segmentation was performed manually to obtain digital contours of each component. Supplemental Fig. 1 presents the selected CT images, and segmented contour plots of the LV, the MV, and the aorta for the modeling construction. Supplemental Fig. 2 gives the stacked CT contours and LV inner/outer surface plots showing the MV and the aorta. Heart rate and blood pressure (arm cuff pressure measurements) at the time of the CT examinations were used in the simulation. Post-operative data was acquired in a similar fashion.

2.3. FSI computational modeling

The material property of the LV was assumed to be hyperelastic, isotropic, incompressible and homogeneous. The modified non-linear Mooney-Rivlin model was used to describe the material properties of LV. The strain-energy function of Mooney-Rivlin model is given by,

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

where $I_1 = \sum C_{ii}$, and $I_2 = \frac{1}{2}(I_1^2 - C_{ij}C_{ij})$ are the first and second strain invariants, $\boldsymbol{C} = [C_{ij}] = \boldsymbol{X}^T\boldsymbol{X}$ is the right Cauchy-Green deformation tensor, $\boldsymbol{X} = [X_{ij}] = [\partial x_i/\partial a_j]$, where x_i is the current position, a_i is the original position, and c_i and D_i are material constants [19,20]. The patient-specific material constants (Supplemental Table 2) were chosen to match the obtained numerical LV volume with the CT-measured LV volume at the end of isovolumic systole for each patient.

Blood flow in the LV was assumed to be laminar, Newtonian, viscous and incompressible. The density of the blood was assumed to be $\rho = 1\ \mathrm{g \cdot cm^{-3}}$ and the viscosity was assumed to be $0.04\ \mathrm{dyn \cdot cm^{-2}}$. The Navier–Stokes equation with Arbitrary Lagrangian Eulerian formula was used as the governing equation. No-slip boundary conditions and natural force boundary conditions were specified at all interfaces to couple fluid and structure models [19–21].

2.4. Pre-active-contraction phase

Under the in vivo condition, the ventricles were pressurized. As such, the zero-load ventricular geometries, which are necessary for numerical simulations, were not known. A pre-shrink process was then applied in our model to obtain the geometry (start geometry) of LV at a zero-load state [22]. As the inlet pressure increased, the LV expanded in both short-axis and long-axis directions, causing the volume to increase. In this phase, the MV opened and the blood filled into LV. At the end of this phase, LV reached its maximum volume and the pressure was the one measured at the end of the isovolumic systole. Please note that in this simulation the motion of LV is different with the real heart motion. The purpose of the simulation in this phase is to obtain information on both the blood flow and the LV at the end of the isovolumic systole, which will be the starting state for the real active contraction simulation. The results of this first pre-load step were reported in Supplementary Table 3.

2.5. The active contraction

We simulated the LV active contraction from the end of the isovolumic systole to the pre-SAM time point. During this period, the MV was closed while the outlet was kept open. As the pressure increased, the blood was ejected; the volume of LV decreased from the maximum volume to the CT-measured volume at the pre-SAM time point. The active contraction was implemented by specifying the pressure conditions at the outlet and the epicardium of LV. The pressure conditions were adjusted until the difference between the simulation results and the clinical measured data were <5% (Supplemental Table 4). The real LV active contraction motion from the end of the isovolumic systole to the pre-SAM time point was implemented.

2.6. Mesh generation and solution method

A volume component-fitting method was employed to generate meshes [20,21]. The fully coupled FSI model was solved by ADINA (ADINA R&D, Watertown, MA) using unstructured finite elements and the Newton–Raphson iteration method. Mesh analysis was performed for each model by reducing the mesh density in each dimension by 10% until differences between solutions from two consecutive meshes were negligible (<1% in L_2-norm). The optimal element size in each dimension was between 0.05 and 0.1 cm. For each patient, there were around 90,000 elements and 60,000 elements for the solid and fluid model, respectively. More details can be found in our previously published papers [20–22].

2.7. Statistical analysis

The data were expressed as mean ± SD. Paired *t*-test was used to compare the differences between the pre- and post-operative groups. A *P* value <.05 was established as the level of statistical significance. All statistical analysis was performed with SPSS 19 (SPSS Inc., Chicago, Ill).

3. Results

3.1. The pressure difference and shear stress on the MVL decreased significantly after successful surgery

The representative images of the LV 3D-geometry, 3D velocity vector flow, the pressure difference on the coapted MVL, and the shear stress distribution on the MVL before and after successful surgery were shown in Fig. 1. Pre-operative vector flow map showed a narrow stream of ejection flow in the LVOT (Fig. 1, Pre-op 3D vector flow map), which was deflected posteriorly by the septal bulge and overlapped the MVL. A large part of blood flow impacted the MVL on its posterior surface. Following successful procedure, the LVOT was widened and the ejection flow became orderly and away from the MVL (Fig. 1, Post-op 3D vector flow map). Only a very small part of the blood flow struck the posterior surface of the MVL. Before surgery, we noticed that the pressure on the posterior surface of leaflets was higher than that on the anterior surface, and therefore the pressure difference was presumed to be the force driving the anterior motion of MV. To assess the driving force of SAM, the distributions of pressure difference on the coapted MVL at the pre-SAM time point (5% RR interval) were analyzed and compared between pre- and post-operative models (Figs. 1, 2). The mean value of pressure difference was relatively high pre-operatively, but decreased significantly after successful septal myectomy in Group 1 (pre-op: 2.22 ± 1.03 mm Hg versus post-op: 0.35 ± 0.17 mm Hg, $n = 5$, $p = .01$), which coincided with the eliminated SAM we observed. The mean value of shear stress on the MVL also decreased significantly when SAM was abolished (pre-op: $6.38 \pm 1.76\ \mathrm{dyn/cm^2}$ versus post-op: $3.27 \pm 1.3\ \mathrm{dyn/cm^2}$, $n = 5$, $p < .01$) (Figs. 1, 2).