A novel approach to in vivo mitral valve stress analysis

Chun Xu,1 Clay J. Brinster,2 Arminder S. Jassar,1,2 Mathieu Vergnat,1 Thomas J. Eperjesi,1 Robert C. Gorman,1,2 Joseph H. Gorman 3rd,1,2 and Benjamin M. Jackson2

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Xu C, Brinster CJ, Jassar AS, Vergnat M, Eperjesi TJ, Gorman RC, Gorman JH 3rd, Jackson BM. A novel approach to in vivo mitral valve stress analysis. Am J Physiol Heart Circ Physiol 299: H1790–H1794, 2010.—Three-dimensional (3-D) echocardiography allows the generation of anatomically correct and time-resolved geometric mitral valve (MV) models. However, as imaged in vivo, the MV assumes its systolic geometric configuration only when loaded. Customarily, finite element analysis (FEA) is used to predict material stress and strain fields rendered by applying a load on an initially unloaded model. Therefore, this study endeavors to provide a framework for the application of in vivo MV geometry and FEA to human MV physiology, pathophysiology, and repair. We hypothesize that in vivo MV geometry can be reasonably used as a surrogate for the unloaded valve in computational (FEA) simulations, yielding reasonable and meaningful stress and strain magnitudes and distributions.

MATERIALS AND METHODS

MV leaflet strain by sonomicrometry. In four normal sheep, sonomicrometry array localization was used to image a rectangular array of four transducers implanted on the anterior leaflet throughout the cardiac cycle. The details of surgical implantation on cardiopulmonary bypass and the methods of sonomicrometry array localization have been previously described (5). Linear and areal strains were calculated by dividing the rectangular array into two triangles, and the enclosed areas were computed at each time point throughout the cardiac cycle. Isovolumic contraction was taken from end diastole (ED, defined at the peak of QRS complex) to end isovolumic contraction (EIVC, defined as the first time point that the aortic blood pressure increases).

Repeated loading of hybrid human MV. A hybrid model of the normal human MV at midsystole was constructed from 10 healthy adult subjects imaged using real-time three-dimensional (3-D) echocardiography (rt-3DE). These experiments have been previously described (17). The hybrid model was selected so as to represent the “average” or characteristic normal human MV. This anatomically correct hybrid MV geometric model was loaded repeatedly—with the deformed leaflet geometry following the first loading providing the initial unloaded geometry for the second loading step—to assess the strain and deformation expected under initial and subsequent pressure load applications. A total of 8,340 and 4,073 nodes and 16,292 and 7,683 triangular elements represented the anterior leaflet and posterior leaflet, respectively. The triangulated leaflets surfaces were imported into a commercial finite element program (Abaqus/Explicit 6.3, HKS, Pawtucket, RI) to quantify predicted regional stress distributions on the MV leaflets. Leaflet tissue was assumed to be orthotropic and linearly elastic, with Young’s modulus determined from excised porcine MV tissue data (8). Thin shell elements (type S3R) were used. Specific anterior and posterior leaflet properties are indicated in Table 1. All freedom of motion except in-plane rotation was fixed for the annular nodes. The coaptation

### Table 1. Mitral valve material properties used in FEA model

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Anterior Leaflet</th>
<th>Posterior Leaflet</th>
<th>Primary Chordae</th>
<th>Secondary Chordae</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thickness, mm</td>
<td>1.4</td>
<td>1.1</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Cross-sectional area, mm²</td>
<td>—</td>
<td>—</td>
<td>0.4</td>
<td>0.7</td>
</tr>
<tr>
<td>$E_{circ}$, Pa</td>
<td>6.20E +06</td>
<td>2.35E +06</td>
<td>2.20E +07</td>
<td>2.20E +07</td>
</tr>
<tr>
<td>$E_{rad}$, Pa</td>
<td>2.10E +06</td>
<td>1.887E +6</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Poisson’s ratio</td>
<td>0.45</td>
<td>0.45</td>
<td>0.45</td>
<td>0.45</td>
</tr>
<tr>
<td>Density, kg/m³</td>
<td>1.04E +04</td>
<td>1.04E +04</td>
<td>1.04E +04</td>
<td>1.04E +04</td>
</tr>
</tbody>
</table>

FEA, finite element analysis; $E_{circ}$, circumferential modulus of elasticity; $E_{rad}$, radial modulus of elasticity.
tion area between anterior and posterior leaflets was defined as an interface pair to prevent the nodes along coapting surfaces from passing through each other. A small degree of sliding was allowed between two leaflets. Chordae tendineae were represented by strings connecting the papillary muscle tips to the insertion points on the leaflets and modeled by a tension-only stress element (element type T3D2). The nodes of the chordal attachment points on the leaflets were fixed with all degrees of freedom except in-plane motion. Systolic loading was accomplished via the application of an 80-mmHg pressure gradient across the MV. Stress, strain, and displacement were recorded as output variables.

Deformation in human MV under isovolumic in vivo loading. Models of three normal human MV were constructed from rt-3DE, as described previously (17). The models generated at ED and EIVC were rotated and translated in Matlab (The Mathworks, Natick, MA) to minimize the sum of squares difference between leaflet surfaces in each of the \( n = 3 \) paired valves; the aligned models were then analyzed to assess deformation under an in vivo pressure load during isovolumic contraction.

**Statistics.** All results are presented as means ± SD unless otherwise indicated. Geometric comparison of whole MV leaflet models was accomplished once two models were optimally aligned by calculating a mean absolute difference in z-coordinate over the surfaces of valve leaflets [i.e., a standard deviation between \( i = 1 \) to \( m \) MV models compared at the number of points over the surface of the anterior and posterior leaflets (\( n_{AL&PL} \))]

\[
\sigma = \sqrt{\frac{1}{n_{AL&PL}} \sum_{i=1}^{m} (z_i - \bar{z})^2}
\]

All human experiments were approved by the Institutional Review Board, and informed consent was obtained before echocardiography. For all ovine experiments, the animals were cared for in compliance with the Guide for the Care and Use of Laboratory Animals (National Institutes of Health, Revised 2010), and the experimental protocols were approved by the Institutional Animal Care and Use Committee.

**RESULTS**

**MV leaflet strain by sonomicrometry.** There was minimal linear and areal strain through the loading associated with isovolumic contraction: the average linear strain was 0.02 ± 0.01, and average areal strain was 0.04 ± 0.02. Figure 1 demonstrates the linear strain through the cardiac cycle, along with the synchronized aortic blood pressure, in a single representative animal.

**Repeated loading of hybrid human MV.** With pressure loading, the hybrid anatomically correct normal human MV experienced peak von Mises stress of 0.63 MPa. Subsequently, the deformed valve leaflets (with persistent boundary conditions) were reloaded (from a hypothetical stress-free state): peak von Mises stress generated was 0.65 MPa. In addition, stress distribution was qualitatively similar in the second, compared with the first, loading event, as demonstrated in Fig. 2. Stress...
magnitude with the second loading step at all locations on mitral leaflets was within 4% of initial loading. Similarly, as also demonstrated in Fig. 2, strain distribution and peak strain magnitude were similar with the second loading step. Finally, the predicted deformation was small with the repeat loading step: 1.2-mm peak deformation, confirming the relatively constant geometric conformation of the MV leaflets with reloading.

Deformation in human MV under isovolumic in vivo loading. Figure 3 compares a single human MV geometric model generated at ED and EIVC, aligned post hoc to allow for translational and rotational displacement during isovolumic contraction; the other \( n = 2 \) cases demonstrated similar invariance in valve geometry during isovolumic contraction. The mean difference between corresponding points on the leaflet surfaces was just \( 0.53 \pm 0.19 \) mm. The supplemental video (posted with the online version of this article) details the minimal deformation in the conformation of the MV leaflets in the course of isovolumic contraction.

DISCUSSION

One might ask what is the utility of current advanced and complicated FEA models of the MV. Some have used MV FEA to ask what might happen to the in vivo valve if a particular repair or intervention is performed. In general, the approach has been to use highly idealized and simplistic geometric models (though often rigorously complicated material properties and fluid-structure formulations) to analyze ex vivo or anatomically idealized MVs to assess physiology (8); to analyze standardized pathological valves to predict stress distribution and, potentially, the integrity and failure behavior of repair techniques; to “evaluate proposed surgical repairs” using idealized computational models (1, 3, 9, 11, 15, 16, 18, 19), including models that attempt integration of fluid-structure interactions (4, 13); or to evaluate pathological alterations on the function of idealized computational models (2, 10, 12). Alternatively, realistic geometric models of the MV have been rarely used, for instance, to assess the relative contributions of primary and secondary chordae to structural integrity (14). Finally and more conventionally, FEA has been used to test and predict failure of devices for MV repair or replacement (21). Table 2 summarizes these varied approaches and summarizes their respective methods and scientific utility.

These attempts at MV modeling are almost uniformly based on idealized or standardized geometries. In contrast, and more recently, Votta et al. (20) have concerned themselves with complicated, anatomically correct analyses of MV stress prediction but have not addressed the question of the rational basis for supposing that FEA of an already-loaded geometric representation of the MV apparatus will yield realistic predictive values of local leaflet stresses and strains. In fact, though that group from Politecnico di Milano imaged the leaflets, annulus, chordae, and papillary muscles through systole and though they modeled the annulus dynamically in time from rt-3DE images (and incorporated a dynamic annular geometry in their model of progressive loading), they made no attempt to compare their loaded ED MV leaflet geometry with the imaged MV leaflet geometry at EIVC.

Table 2. Applications of FEA models of mitral valve

<table>
<thead>
<tr>
<th>Approach</th>
<th>Utility and Features</th>
<th>References Using Approach</th>
</tr>
</thead>
<tbody>
<tr>
<td>Analysis of in vivo valves</td>
<td>• Applicable clinically to individual human patients</td>
<td>14, 20</td>
</tr>
<tr>
<td>Prediction of repair integrity and longevity</td>
<td>• Potentially useful for design of repair techniques</td>
<td>1, 3, 4, 9, 11, 13, 15, 16, 18, 19</td>
</tr>
<tr>
<td>Testing of device performance</td>
<td>• Conventional industrial use of FEA</td>
<td>21</td>
</tr>
<tr>
<td>Physiology of normal or pathological valve</td>
<td>• Theoretical physiological study</td>
<td>2, 10, 12</td>
</tr>
<tr>
<td>Other</td>
<td>• Inverse determination of material properties from in vivo invasive imaging</td>
<td>6, 7</td>
</tr>
</tbody>
</table>
In the current work, the first set of experiments, MV leaflet strain by sonomicrometry, demonstrates that leaflet strain is minimal during isovolumic contraction and hence during pressure loading of the left ventricle. Hence, we expect that the deformation of the valve and its leaflets is small during loading, so that MV models generated by noninvasive imaging (e.g., cardiac MRI, cardiac computed tomography, or rt-3DE) of the pressure-loaded valve may from a geometric standpoint be appropriately used in FEA work as unloaded valve geometries.

The second set of experiments, Repeated loading of hybrid human MV, uses a rigorously defined (high-resolution 3-D imaging-derived model) MV geometry and FEA. The midystemic valve is repeatedly loaded, with the deformed leaflet geometry of the first loading providing the initial (unloaded or stress-free) geometry for the second loading. Using the loaded geometry of the MV as the input for a physiological (left ventricular pressure load) FEA (second loading event) provides very similar (within 4% at all locations over both leaflet surfaces) stress results as does loading the initial MV model (first loading event). Hence, reloading (in FEA) a MV model generated from imaging a physiologically (in vivo) loaded valve is not unreasonable and is expected to provide meaningful stress and strain measures.

In the final experiments, Deformation in human MV under isovolumic in vivo loading, there was minimal deformation in the valve geometry during pressure loading. Because left ventricular volume is constant during isovolumic contraction, the structures (the base of the ventricle, the papillary muscles, and the fibrous trigone of the heart) constraining the valve are relatively static. Therefore, deformations in leaflet geometry during this portion of the cardiac cycle are most likely due to pressure loading. That minimal deformation confirms the hypothesis that the loaded in vivo MV geometry can be reasonably used as a surrogate for the unloaded valve in computational (FEA) simulations.

Others’ measurement of MV leaflet material properties can be compared with the results herein presented. In results similar to our demonstration, using sonomicrometry, that mitral leaflet surface strain during loading is minimal relative to the large-scale anatomic and geometric changes in surface geometry (shape), Krishnamurthy et al. (6) found unexpectedly high coefficients of elasticity of the ovine anterior MV leaflet in a study using biplane marker angiography and FEA solutions. With their value of 11 MPa for the radial modulus of elasticity, a peak systolic pressure of 80 mmHg, and a mitral leaflet with a local radius of curvature of 1 cm and a thickness of 1 mm, one would expect only a maximal strain of 0.01; this value is very close to our measured leaflet strain. (The circumferential modulus of elasticity measured in the Krishnamurthy work was greater, 43 MPa, but is of the same order of magnitude.)

Drawbacks of the current study include a less-than-comprehensive MV model: 1) whereas the leaflet surface profile is accurately determined by rt-3DE, chordae tendineae and papillary muscles were not reliably imaged and so their incorporation in the model is, at best, heuristically motivated; and 2) the material properties model used is far from as comprehensive or, presumably, realistic as others previously published. The material properties—the linear orthotropic leaflet Young’s moduli were used—are simplified; however, the small strains measured in both the sonomicrometry and FEA repeated loading experiments would seem to justify using linear material properties. In fact, Krishnamurthy et al. (7) found that the anterior leaflet of the MV demonstrates a fairly linear stress-strain relationship during isovolumic relaxation. Furthermore, these potential drawbacks are irrelevant to the stated aims and robust conclusions of the study: the goal was not to create a religiously accurate MV FEA model, but rather to justify the FEA approach for analysis and stress prediction of in vivo, noninvasively imaged MV models. (This situation is most often of clinical relevance, in humans who cannot or will not undergo invasive imaging, experimental valve loading experiments, leaflet strain measurements, or ex vivo valvular analyses.) As such, the current experiments justify the application of any MV FEA model, in particular the elegant and more fully developed and validated models of Kunzelman et al. (13) or Prot et al. (14).

Therefore, given the results of the current experiments, a rational approach to in vivo MV stress analysis would incorporate realistic, anatomically resolved, empiric material properties of leaflets and chordae, in vivo high-resolution truly 3-D imaging for geometric model determination, and FEA modeling. In particular, future experiments, incorporating more realistic material properties, will hopefully assess the relative contributions of material properties, pressure load, and geometry in the in vivo human MV.

GRANTS
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DISCLOSURES
No conflicts of interest, financial or otherwise, are declared by the author(s).

REFERENCES