Posterior Papillary Muscle Anchoring Affects Remote Myofiber Stress and Pump Function: Finite Element Analysis

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Background. The role of posterior papillary muscle anchoring (PPMA) in the management of chronic ischemic mitral regurgitation (CIMR) is controversial. We studied the effect of anchoring point direction and relocation displacement on left ventricular (LV) regional myofiber stress and pump function.

Methods. Previously described finite element models of sheep 16 weeks after posterolateral myocardial infarction (MI) were used. True-sized mitral annuloplasty (MA) ring insertion plus different PPM anchoring techniques were simulated. Anchoring points tested included both commissures and the central anterior mitral annulus; relocation displacement varied from 10% to 40% of baseline diastolic distance from the PPM to the anchor points on the annulus. For each reconstruction scenario, myofiber stress in the MI, border zone, and remote myocardium as well as pump function were calculated.

Chronic ischemic mitral regurgitation (CIMR) is caused by left ventricular (LV) remodeling that occurs typically after posterolateral myocardial infarction (MI). CIMR is a significant problem causing congestive heart failure and decreased survival [1–3].

The standard surgical treatment for CIMR is reduction mitral annuloplasty (MA). Although patients with unrepaired mild to moderate CIMR are at increased risk of repeated hospitalization and death [4], the efficacy of MA at the time of coronary bypass grafting (CABG) remains unclear. The Randomized Ischemic Mitral Evaluation trial was stopped early with a greater improvement in peak oxygen consumption in the CABG + MA group [5], and a National Institute of Health–sponsored trial of CABG ± MA for patients with moderate CIMR is under way.

However, CIMR repair with reduction MA may have associated recurrence in up to 32% of patients [6–8]. These failures are caused by the progressive LV enlargement with further displacement of the posterior papillary muscle (PPM) [7]. Therefore, although reduction annuloplasty may be able to initially correct MR, it may not stop or reverse negative LV remodeling, particularly in larger ventricles [9, 10].

As a consequence, a number of “subvalvular” procedures have been proposed. PPM stabilization has been advocated by proponents of papillary muscle banding [11], whereas others have favored anchoring the PPM to anterior ventricular structures. Examples include (1) a suture placed between the PPM and the right posterior mitral annulus as proposed by Kron and coworkers [12], (2) a suture between the PPM and the right fibrous trigone region of the anterior mitral annulus as described by Langer and colleagues [13], and (3) a suture placed between the lateral and anterior LV walls as in the case of the Coapsys LV reshaping device (Myocor, Inc, Maple Grove, MN) [14]. Although it is believed that these procedures acutely reshape the left ventricle and provide long-term stabilization, it is unknown whether they provide remote myofiber stress reduction.

This study used validated finite element models of the ovine mitral apparatus and ventricle to quantify the acute effects of various PPM relocation techniques. Specifically, the different techniques of anchor point location and the

Accepted for publication April 15, 2014.

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amount of displacement (relocation distance) were studied. We hypothesized that greater PPM displacement and anchoring at the anterior commissure would produce the greatest decreases in remote myofiber stress.

Material and Methods

Animals used in this study were treated in compliance with the “Guide for the Care and Use of Laboratory Animals.” Five male adult Dorset sheep underwent posterolateral MI as previously described [15], with magnetic resonance imaging (MRI) performed at 16 weeks after MI, allowing construction of 5 finite element models as previously reported [16, 17]. LV myocardium was divided into MI, border zone, and remote myocardium, in which the border zone–remote boundary was defined as the point at which wall thickness is 70% of the maximum LV wall thickness. The mitral apparatus was simply modeled as described by Wenk and colleagues [18, 19]. Mitral leaflets were modeled using B-spline curves that estimated leaflet contours. Edge chords were attached to the free edge of each leaflet and strut chords were attached to the midsection of each leaflet (Fig 1). To isolate the mitral valve (MV) apparatus from boundary condition interactions, the basal myocardial nodes were extended above the MV plane and basal epicardial nodes were fully constrained. Simulations were performed on a Linux cluster.

Loading and Constitutive Models

The endocardial wall was loaded to the measured in vivo end-diastolic and end-systolic LV pressures. The mitral leaflets were loaded with a pressure of -1.125 mm Hg to simulate a pressure gradient from the left atrium to the left ventricle throughout diastole. To simulate an outward pressure from the left ventricle, leaflets were loaded with measured in vivo end-systolic LV pressures throughout systole. Active and passive myocardial constitutive laws, previously described by Guccione and associates [20, 21], were implemented with a user-defined material subroutine (LS-DYNA; LSTC, Livermore, CA). Passive stiffness and contractility material properties were optimized to match end-diastolic and end-systolic volumes of each animal-specific finite element model to its respective experimental volumes. Average material values and comparison of individual model and matched experiment are detailed in the Appendix. The MV leaflets and aortic root cap were modeled with LS-DYNA material properties for soft tissue (*MAT_091), whereas the chordae tendineae were modeled with cable elements (*MAT_071).

Posterior Papillary Muscle Anchoring

PPMA was performed using a virtual suture method, with the suture modeled as a cable beam carrying a predefined tension with a Young’s modulus of \( E = 1.0 \times 10^6 \) kPa to minimize stretching. The anchor was attached to the 4 surface nodes closest to the chordal attachment of the PPM. The other end of the anchor was either the anterior commissure (AC) and the posterior commissure (PC) or the center point (CP) along the anterior annulus (Fig 1). The relocation distance ranged from 10% to 40% of the unshortened diastolic length of the anchor suture.

Mitril Annuloplasty

Virtual MA was performed as previously described [22]. Briefly, a saddle-shaped MA ring (Carpentier-Edwards Physio II, size 24; Edwards Lifesciences, Irvine, CA) was modeled from B-spline curves and sized true for each

Abbreviations and Acronyms

AC = anterior commissure
APSA = anterior-posterior short axis
CABG = coronary artery bypass grafting
CIMR = chronic ischemic mitral regurgitation
CP = center point
LV = left ventricular
MA = mitral annuloplasty
MI = myocardial infarction
PC = posterior commissure
PPM = posterior papillary muscle
PPM→PC = distance vector from the PPM to the posterior commissure
PPMA = posterior papillary muscle anchoring
SLSA = septal-lateral short axis

Fig 1. Posterior papillary muscle anchoring (PPMA) suture was placed between the PPM and either the anterior commissure (AC), posterior commissure (PC), or the center point (CP) anterior annulus anchor points. The dashed line occurs where the solid line passes behind the PPM papillary muscle. The PPM position was tracked by measuring PPM→PC.
sheep by scaling to the commissure-to-commissure distance. Thirty-two virtual sutures were evenly placed between the ring and mitral annulus (Fig 2), with axial tensioning effectively drawing the mitral annulus toward the ring.

**Measured Outcomes**

After each simulated condition, the septal-lateral short axis (SLSA) and the anterior-posterior short axis (APSA) were measured at end-systole. Additionally, the distance vector from the PPM to the PC (PPM→PC) and its directional components were measured. Regional myocardial fiber stresses in the MI, border zone, and remote myocardium were calculated; additional representative sections of the remote myocardium (anterior remote zone, septal remote zone, and lateral remote zone) were analyzed. The mitral leaflet coaptation depth was measured as the distance from the MV plane to the top of the coaptation zone. Finally, stroke volume was measured.

**Statistical Analysis**

All values are expressed as mean ± standard deviation and compared by repeated measures analysis using a mixed model to test for both fixed and random effects (PROC MIXED, SAS system for Windows, version 9.3; SAS Institute, Cary, NC). The impacts of anchoring point, displacement, and an interaction factor were tested on regional myocardial displacement, and an interaction factor were tested on fiber stress and stroke volume. Displacement was tested as either proportional or absolute PPM displacement. The animal was held as a random variable and the MA case for each sheep was used as a control. Significance was set at $p < 0.05$.

![Sutures Annuloplasty](Image)

**Results**

**PPM Anchoring—Direction and Distance**

Baseline PPM→PC diastolic distances were $2.64 ± 0.61$ cm, $1.52 ± 0.58$ cm, and $1.05 ± 0.58$ cm in the basal-apical, anterior-posterior, and septal-lateral directions, respectively. All tested conditions resulted in a basal, septal, and anterior relocation of the PPM toward the mitral annulus ($F = 35.16, F = 33.17, F = 14.55$, respectively; $p < 0.0001$ for all). The AC direction had the greatest basal and anterior displacements, whereas the central anterior annulus direction had the greatest septal displacement (Fig 3).

**Effect on LV Shape**

All PPM relocations with displacements greater than 10% decreased SLSA compared with MA ($F = 13.36; p < 0.0001$) and was weakly associated with anchoring direction ($F = 3.20; p = 0.0505$), with the CP anchor point causing the greatest SLSA decrease. APSA did not decrease compared with MA ($F = 0.27; p = 0.9934$) and was not correlated with changes in anchor point ($F = 0.69; p = 0.5065$) or displacement ($F = 0.05; p = 0.9843$).

**Effect on Regional Myofiber Stress**

Regional myocardial stress at end-diastole and end-systole significantly decreased with all displacement and anchor point combinations, except 10% displacement, compared with the MA (Fig 4). Furthermore, myofiber stress reductions varied regionally, with maximal PPM displacement affecting the MI region the most (diastolic: $1.396 ± 0.2399$ kPa; systolic: $8.6659 ± 1.3140$ kPa) and the remote myocardium the least (diastolic: $0.09805 ± 0.0094$ kPa; systolic: $1.0259 ± 0.1242$ kPa). Regional myofiber stress was significantly decreased by increasing displacement ($p < 0.0001$ in all regions). However, significance was lost when controlling for SLSA (MI: $p = 0.8168$; border zone: $p = 0.9953$; remote zone: $p = 0.3737$), whereas SLSA was significantly correlated with myofiber stress (MI: $F = 35.96, p < 0.0001$; border zone: $F = 13.95, p = 0.0005$; remote zone: $F = 33.95, p < 0.0001$). Therefore, decreasing SLSA, which was achieved through PPMA, was the direct mediating factor in myofiber stress reduction and not displacement. Anchor point location also affected regional myofiber stress (MI: $p = 0.0028$; border zone: $p = 0.0010$; remote zone: $p = 0.0004$). However, significance was lost after controlling for absolute displacement (instead of percent displacement) (MI: $p = 0.5996$; border zone: $p = 0.5054$; remote zone: $p = 0.998$). With maximal PPM displacement, peak systolic and diastolic changes in stress in remote regions included decreases of 11.03% and 23.38% for the anterior remote zone and 3.60% and 4.93% for the lateral remote zone and increases of 2.11% and 5.22% for the septal remote zone.

**Effect on Mitral Leaflet Position**

All PPMA scenarios with displacements greater than 10% reduced coaptation depth compared with MA ($F = 9.38;
There was a significant reduction in coaptation depth with increasing displacement ($F = 25.68; p < 0.0001$), with 40% displacement causing the coaptation zone to move $0.25 \pm 0.14$ cm above the annular plane. Finally, anchor point location was not associated with changes in coaptation depth ($F = 0.05; p = 0.9541$).

**Effect on Pump Function**

All PPMA scenarios with displacements greater than 10% significantly reduced end-diastolic volume ($F = 35.32; p < 0.0001$) and end-systolic volume ($F = 24.92; p < 0.0001$) compared with MA (Figs 6A, 6B). Additionally, only scenarios with a maximal 40% displacement caused a significant reduction in stroke volume ($F = 6.83; p < 0.0001$). However, if correction of CIMR by MA + PPMA is assumed to prevent regurgitant volume, there was an overall increase in forward stroke volume ($F = 1.24; p = 0.2987$), or end-systolic volume ($F = 0.24; p = 0.7877$) after controlling for absolute displacement.

**Comment**

The principal finding of this study is that PPM anchoring causes a reduction in myofiber stress at end-diastole and end-systole in MI, border zone, and remote regions of the left ventricle that is proportional to the percentage displacement but independent of anchor point location.

**Anchor Point Direction**

Anchor point location affected myofiber stress when the degree of PPMA was measured as a proportional displacement but did not reduce stress when PPMA was measured as an absolute displacement. In other words, the absolute distance of PPM displacement was more important than the direction to which it was drawn. Anchor point affects both the magnitude and direction of PPMA displacement and has implications for MV function and CIMR. This was demonstrated most clearly in the study by Langer and colleagues [23] in which PPMA relocation toward the posterior and anterior commissures alone and in combination was studied in sheep. In their series, only PPMA→PC caused...
displacement of the PPM toward the mitral annulus. Although Langer and associates [13, 23] adjusted PPMA suture tension in this and subsequent studies to observed effect, it appears that this relocation corresponds approximately to only our 10% displacement data.

**Reductions in Regional Myofiber Stress**

There is no consensus in animal and clinical studies about the ability of mitral valve repair to reverse the LV remodeling that occurs with CIMR. Matsuzaki and colleagues [24] found that mitral annuloplasty does not affect remodeling when performed 8 weeks after posterolateral MI in sheep [24]. In contrast, Beeri and associates [25] demonstrated return to baseline LV volume when left atrial to LV shunt (MR equivalent) was occluded 6 weeks after MI. Although LV size and ejection fraction are significantly improved in patients with CIMR who are treated with CABG + MV repair [26], mortality is not improved [27, 28].

LV enlargement (remodeling) after MI is a consequence of infarct expansion, extension of the infarct border zone [29], hypertrophy of the remote myocardium, and the effects of neurohumoral compensatory pathways [30]. Of these, infarct expansion, border zone extension, and remote zone changes are thought to be mediated by wall stress. It is possible that when PPMA-mediated reduction in stress is added to the reduction in end-diastolic stress that occurs when the MV becomes competent, LV reverse remodeling (reduction in LV volume) will accelerate after mitral repair for CIMR.

The mediocre postoperative stress reductions mediated by reductions in SLSA observed in our study may also account for the unique improved mortality observed in
the RESTORE-MV trial of the Coapsys device [31]. In a recent finite element study of the Coapsys device, the increase in 1-year survival rate with Coapsys compared with MA was postulated to be attributable to the sizable stress reduction achieved after ventricular shape change [32]. Significantly and unfortunately, PPMA in this experimental series did not effect major changes in LV geometry vis-a-vis remote myocardial stress reduction as demonstrated with Coapsys reshaping, in which reductions of 53% in diastole and 32% in systole were noted. This is at least an order of magnitude greater than the 9% diastolic and 7% systolic changes in remote myocardial stress noted here by pulling on the PM tip. Whether a more radical PM and injured ventricular wall reshaping will produce more favorable remote myocardial stress changes is unknown and should be the subject of future investigations.

Effect on Mitral Valve Geometry
What this study does affirm are the favorable leaflet changes that result in improved coaptation depth. The coaptation depth or “tenting” of the repaired valves clearly decreased proportionately with PPM displacement. As reconfirmed in the recent Cardiothoracic Surgical Trials Network study of CIMR operations [6], recurrent MR remains a significant issue with a repair strategy; it was present in 32.6% of survivors (moderate MR, 28.4% ; severe MR, 4.2%) at 1 year. Unfortunately,
no information regarding the baseline ventricular dimensions in the “recurring” patients was given. We could speculate that the decrease in tenting depth associated with PPMA might decrease the incidence of recurrent MR in this vulnerable population. The unresolved issue is whether these changes will persist and help reduce recurrent MR. If they are only temporary, those ventricles with significant ventricular injury will continue to negatively remodel, disrupting a repair and producing recurrent MR. The degree of long-term “resiliency” PPMA clinically adds to a CIMR repair remains unknown.

Effect on Pump Function

PPMA in which anchor point to PPM distance was reduced by 40% caused a slight reduction in LV pump function. Although PPMA reduced both end-systolic volume and end-diastolic volume, the reduction in stroke volume was primarily driven by end-diastolic volume. This is similar to the reduction in pump function in other procedures that reshape the left ventricle [33] and in LV volume reduction procedures [34]. However, as with the Coapsys device [32], if correction of CIMR by MA + PPMA is assumed, there was an overall increase in forward stroke volume.

Study Limitations

Several assumptions were incorporated into the model. First, the fiber direction was uniform throughout the PM (aligned to the apical-basal direction) and based on the previous computational models [18]. The central surface of the PPM bodies were used as chordal attachment points; finer modeling of the papillary trunks was not available. Furthermore, the finite element model did not incorporate fluid-structure interactions. Thus, the surgical effects on regurgitant volumes were not directly measured. It was assumed that MA and PPMA successfully eliminated MR. Preoperative regurgitant volumes were estimated as the in vivo difference between left and right ventricular systolic volume.

Conclusions and Future Directions

PPMA causes a reduction in myoﬁber stress in all regions of the left ventricle that is proportional to the degree of tightening, with only small reductions noted in the remote myocardium. It is unknown whether such modest remote stress reductions may arrest or mitigate negative LV remodeling. PPMA does improve leaflet tethering, but its persistence and potential to diminish recurrent MR is unknown. With variations in PPMA procedures and few systematic investigations, virtual surgery methodology will continue to provide procedural analysis and allow for optimization of strategies.

This study was supported by National Institutes of Health grant R01-HL-63348 (MBR) and by AHA grant 13MSRF17090108. This support is gratefully acknowledged.

References


Ann Thorac Surg
2014;98:1355–62

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ADULT CARDIAC

References


Appendix. Applied Material Properties and Model Comparisons

A. Diastolic material values, \(\sigma_f = 49.25\), \(\sigma_t = 19.25\), \(\sigma_{fs} = 17.44\), were used for all regions

B. Regionally varying averaged material properties

<table>
<thead>
<tr>
<th></th>
<th>Passive Stiffness, C (kPa)</th>
<th>Contractility, (T_{max}) (kPa)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Remote zone</strong></td>
<td>0.0298 ± 0.02</td>
<td>203.05 ± 51.43</td>
</tr>
<tr>
<td><strong>Border zone</strong></td>
<td>0.0298 ± 0.02</td>
<td>61.29 ± 17.44</td>
</tr>
<tr>
<td><strong>Infarct</strong></td>
<td>0.298 ± 0.23</td>
<td>0 ± 0</td>
</tr>
</tbody>
</table>

C. Comparison between experimental (MRI) and finite element model left ventricular (LV) volumes is presented in the following table. Regurgitant volume was estimated as the in vivo difference between LV and right ventricular stroke volumes.

<table>
<thead>
<tr>
<th></th>
<th>End-Diastolic Volume (mL)</th>
<th>End-Systolic Volume (mL)</th>
<th>Stroke Volume (mL)</th>
<th>Regurgitant Volume (mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Preoperative MRI</strong></td>
<td>91.56 ± 12.72</td>
<td>52.98 ± 12.2</td>
<td>38.58 ± 5.28</td>
<td>14.4 ± 5.46</td>
</tr>
<tr>
<td><strong>Finite element preoperative model</strong></td>
<td>92.3 ± 17.09</td>
<td>56.9 ± 10.53</td>
<td>35.4 ± 13.53</td>
<td>NA</td>
</tr>
</tbody>
</table>

MRI = magnetic resonance imaging; NA = not available.