Importance of Mitral Valve Second-Order Chordae for Left Ventricular Geometry, Wall Thickening Mechanics, and Global Systolic Function

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Background—Mitral valvular–ventricular continuity is important for left ventricular (LV) systolic function, but the specific contributions of the anterior leaflet second-order “strut” chordae are unknown.

Methods and Results—Eight sheep had radiopaque markers implanted to silhouette the LV, annulus, and papillary muscles (PMs); 3 transmural bead columns were inserted into the mid-lateral wall between the PMs. The strut chordae were encircled with exteriorized wire snares. Three-dimensional marker images and hemodynamic data were acquired before and after chordal cutting. Preload recruitable stroke work (PRSW) and end-systolic elastance (Ees) were calculated to assess global LV systolic function (n = 7). Transmural strains were measured from bead displacements (n = 4). Chordal cutting caused global LV dysfunction: Ees (1.48 ± 1.12 versus 0.98 ± 1.30 mm Hg/mL, P = 0.04) and PRSW (69 ± 16 versus 60 ± 15 mm Hg, P = 0.03) decreased. Although heart rate and time from ED to ES were unchanged, time of mid-ejection was delayed (125 ± 18 versus 136 ± 19 ms, P = 0.01). Globally, the LV apex and posterior PM tip were displaced away from the fibrous annulus and LV base-apex length increased at end-diastole and end-systole (all +1 mm, P < 0.05). Locally, subendocardial end-diastolic strains occurred: Longitudinal strain (E12) 0.030 ± 0.013 and radial thickening (E11) 0.081 ± 0.041 (both P < 0.05 versus zero). Subendocardial systolic shear strains were also perturbed: Circumferential-longitudinal “micro-torsion” (E21) (0.099 ± 0.035 versus 0.075 ± 0.025) and circumferential radial shear (E33) (0.084 ± 0.023 versus 0.039 ± 0.008, both P < 0.05).

Conclusion—Cutting second-order chords altered LV geometry, remodeled the myocardium between the PMs, perturbed local systolic strain patterns affecting micro-torsion and wall-thickening, and caused global systolic dysfunction, demonstrating the importance of these chordae for LV structure and function. (Circulation. 2004; 110[suppl II]:II-115–II-122.)

Key Words: contractility ■ mechanics ■ mitral valve ■ regurgitation ■ structure

The mitral subvalvular apparatus consists of the papillary muscles (PMs) and 2 major sets of chordae: (1) first-order (primary or “marginal”) chordae, which insert on the leaflet-free edges; and (2) second-order chordae, which are larger and fewer in number, that insert on the ventricular surface of the anterior leaflet belly at the junction of the rough and smooth zones, and often include 2 thick basal or “strut” chordae.1 This subvalvular apparatus performs a dual role, both maintaining valvular competence and enhancing left ventricular (LV) systolic pump function. The importance of mitral papillary–annular continuity for optimal global LV systolic performance, a concept we have previously termed “valvular–ventricular interaction,”2,3 has been demonstrated in clinical studies showing improved patient outcomes and LV performance after chordal preservation during mitral valve replacement2–4 and in experimental studies documenting global LV contractile dysfunction after transection of all chordae.2,5 Mitral valve repair is associated with superior...
survival and improved LV function compared with replacement, in part because the entire subvalvular apparatus is preserved.

Although the importance of chordal preservation for LV systolic function during valve replacement is widely accepted, the selective roles of first-order versus second-order chordae have only recently been explored. In a study of isolated porcine hearts, Obadia et al showed that transection of the first-order chordae resulted in leaflet prolapse and mitral regurgitation (MR) without affecting circumferential segmental shortening along the mid-anterolateral LV wall. Conversely, cutting the second-order chordae decreased fractional segment shortening and forward aortic flow but did not result in MR. These authors first suggested different roles for the first-order and second-order chordae, with the first-order chordae preventing leaflet prolapse and the second-order chordae involved in ventricular mechanics. Kunzelman et al reported differences in first-order and second-order chordae material properties, which may reflect these specific roles: First-order chordae are stiffer (ie, less extensible), consistent with preventing leaflet prolapse, whereas the larger, more elastic second-order chordae may mediate valvular–ventricular interaction. Nonetheless, cutting second-order chordae has recently been proposed as a therapeutic intervention for patients with ischemic MR to reduce leaflet apical tethering.

The selective roles of first-order versus second-order chordae are important for LV systolic function, then they may be even more so in the setting of ischemic MR in hearts that are already impaired. Although we believe that the second-order chordae are important for valvular–ventricular interaction, debate exists because reports from a previous experiment in this laboratory failed to demonstrate changes in either load-dependent or load-independent indices of global LV function after transection of second-order chordae, and Messas et al observed no change in LV ejection fraction after chordal cutting. Alterations in regional LV systolic dysfunction (decreased fractional area shortening and decreased regional preload recruitable stroke work) adjacent to the PM insertion sites, however, have been observed. We sought to clarify these issues and address the limitations inherent in our earlier experiment by measuring global LV function and transmural systolic LV wall mechanics before and after transection of the second-order chordae.

Materials and Methods

All animals received humane care in compliance with the Principles of Laboratory Animal Care formulated by the National Society for Medical Research and the Guide for Care and Use of Laboratory Animals prepared by the National Academy of Sciences and published by the National Institutes of Health (DHHS NIH publication 85-23, revised 1985). This study was approved by the Stanford Medical Center Laboratory Research Animal Review committee and conducted according to Stanford University policy.

Surgical Preparation

Twenty-two Dorsett hybrid sheep (74±10 kg) were premedicated with ketamine (25 mg/kg intramuscularly). Anesthesia was induced with sodium thiopental (6.8 mg/kg intramuscularly) and maintained with inhalational isoflurane (1.5% to 2.2%). Working through a left thoracotomy, epicardial echocardiography was used to identify a region of the mid-lateral LV wall between the PMs at the equatorial level. After end-diastolic wall thickness was measured (10±1 mm), 3 transmural columns of 3 lead beads each (0.7-mm diameter) were inserted between the PMs spaced evenly from subendocardium to subepicardium using a similar method as originally described by Waldman et al. An 1-cm-thick Plexiglas template was sutured to the equatorial PM inserting into the anterior mitral leaflet (AML) belly was identified (ie, the 2 most central “strut” chordae), and wire snares (insulated except where they encircled the chordae) were secured around these chordae and exteriorized through the LV wall. Extreme care was taken to ensure that the snares did not inadvertently trap any first-order chordae. Markers were placed on each PM tip near the origin of the strut chordae (22 and 23; Figure 1). A micromanometer-tipped catheter (Millar SPC-500; Millar Instruments, Inc) was inserted through the LV apex to monitor LV pressure (LVP),
Animals were weaned from CPB and received intravenous magnesium (3 g), lidocaine (100 mg), and bretylium (50 mg) before transfer as prophylaxis against rhythm disturbances. Epicardial color Doppler echocardiography confirmed normal leaflet motion and valvular competence.

**Experimental Protocol**

Immediately postoperatively, animals were transferred to the catheterization laboratory and studied with the chest open; maintenance anesthesia was continued with inhalational isoflurane (1.5% to 2.2%). Sequences of bivocal videofluoroscopic and hemodynamic data were acquired over a physiological range of LV filling volumes during transient vena caval occlusion with animals in the right lateral decubitus position and ventilation briefly arrested at end-expiration (to prevent respiratory variation). Before baseline data acquisition, transient posterolateral ischemia (53±49 seconds) was induced by mid-circumflex coronary artery occlusion for another experiment. After this ischemic interval, the animals were allowed to stabilize for 5 minutes. Baseline data were then acquired with the second-order chords intact (pre-cut). Before chordal cutting, animals received an additional 100 mg of lidocaine (intravenous) as prophylaxis against rhythm disturbances. The strut chords were then immediately divided by passing electrocautery RF current through the externalized wire snare (cut). After chordal cutting, the animals were allowed to stabilize for 5 minutes, and then data were acquired (postcut). Simultaneous transesophageal color Doppler echocardiography allowed evaluation of the degree of MR before and after cut by an experienced echocardiographer (D.L.) on a 0 to +4 scale (none, mild, moderate, moderate–severe, and severe).

**Data Acquisition**

A Philips Optimus 2000 bivocal Lateral ARC 2/poly DIAGNOST C2 system (Philips Medical Systems) was used to record videofluoroscopic images at 60-Hz. Two-dimensional images from the 2 x-ray views were digitized using custom software.16 These data were merged to yield 3-dimensional coordinates for each radiopaque marker every 16.7 ms, the accuracy of which is 0.1±0.3 mm compared with known marker-to-marker 3-dimensional lengths.17 Analog LVP and ECG signals were digitized simultaneously and recorded on videotape along with marker images during data acquisition.

**Data Analysis**

Of 22 animals entered into this experiment, 8 had successful transection of second-order strut chordae without damage to first-order chordae or AML and without ventricular fibrillation during the cutting attempt. These 8 animals comprise the present study group. Six other animals had inadvertent damage to first-order chords (which was evident immediately on echocardiography and confirmed on necropsy), and 8 other sheep fibrillated during the cutting attempt; thus, 14 animals were excluded.

End-diastole (ED) was defined as the time of maximum second derivative of LVP, corresponding with the frame immediately before the upstroke of LVP. End-systole (ES) was defined as the videofluoroscopic frame before the time of peak negative LV rate of pressure fall (∼dP/dtmin). Hemodynamic and marker-derived data from 3 consecutive steady-state beats in sinus rhythm were time-aligned at ED and averaged for each animal before (precut) and after (postcut) strut chord transection.

Instantaneous LV volume was calculated from LV and MA markers using multiple tetrahedra constructed from the marker coordinates and corrected for LV convexity.18 Although epicardial LV volume calculated in this manner overestimates true LV chamber volume (because it incorporates LV muscle mass), changes in this “epicardial” LV volume are an accurate measurement of the relative changes in LV chamber volume because LV muscle mass remains constant throughout the cardiac cycle. Stroke volume (SV) was calculated as the difference between end-diastolic LV volume (EDV) and end-systolic LV volume (ESV): $SV = EDV - ESV$. Mid-

![Figure 2](image)

**Figure 2.** End-systolic elastance (a). Representative pressure–volume loops obtained during cava occlusion before (precut; black circles) and after (postcut; gray triangles) cutting the anterior mitral valve leaflet second-order chordae. Each dot represents an actual pressure–volume datum, with successive points being 16.7 ms apart in time. In each sheep there was a rightward and downward shift of the end-systolic pressure–volume relationship along with a decline in the slope ($E_{es}$) after chordal cutting. Left ventricular pressure (LVP; mm Hg) is on the ordinate and left ventricular volume (mL) on the abscissa. Preload recruitable stroke work (b). End-diastolic volume-stroke work relationship (preload recruitable stroke work [PRSW]) obtained during cava occlusion before (precut; black circles) and after (postcut; gray triangles) cutting the anterior mitral valve leaflet second-order chordae in all animals. In each animal, the slope of PRSW fell after chordal cutting, indicating reduced external pressure–volume work generated at any given level of left ventricular preload. Left ventricular stroke work (mm Hg · mL) is on the ordinate and left ventricular end-diastolic volume (mL) on the abscissa.

Ejection was defined at the time when one-half of stroke volume had been ejected.

In 7 of the 8 sheep with successful cut, satisfactory vena cava occlusions during data acquisition allowed calculation of load-independent indices of LV function, end-systolic elastance ($E_{es}$), and preload recruitable stroke work (PRSW).5 Three steady-state beats and 2 occlusion beats were analyzed for each animal.

The end-systolic pressure-volume relationship (ie, end-systolic elastance) was calculated to measure global LV systolic mechanics (contractility) as follows: LV end-systolic pressure ($P_{es}$) and volume ($V_{es}$) points were determined at the upper-left hand corner of the PV loop for each cardiac cycle analyzed during preload alteration (Figure 2a). By least-squares linear regression, a line was fitted to these points:

$$P_{es} = E_{es}(V_{es} - V_o)$$

where $E_{es}$ and $V_o$ are the slope and volume axis intercept, respectively.20

Another load-insensitive measure of LV performance, PRSW, which incorporates both systolic and diastolic conditions, was determined by relating stroke work (SW) to EDV (Figure 2b). Stroke work was calculated as the integral of LV pressure (P) multiplied by change in volume (dV):

$$SW = \int P \cdot dV$$

over each cardiac cycle for the steady-state and occlusion beats. PRSW was then obtained by linear regression of SW on EDV as:

$$SW = M_o(EDV - V_o)$$
where $M_a$ and $V_a$ are the slope and volume axis intercept, respectively, of the regression line.\(^{27}\)

Distances at ED and ES were calculated for precut and postcut conditions using 3-dimensional marker coordinates. Without assumption of planar geometry, the centroid of 4 MA markers (ie, the sutured horn, anterior commissures, posterior commissures, and lateral MA markers; 14, 16, 20, and 18, respectively; Figure 1) was determined and LV longitudinal length was measured between the MA centroid and the apical marker. Similarly, individual distances between the LV apex and MA sutured horn, LFT, RFT, anterior commissures, posterior commissures, and lateral markers were calculated to assess changes in these lengths. Distances between the septal and lateral wall markers and between anterior and posterior wall markers were measured at annular, LV basal, equatorial, and apical levels (Figure 1) to determine changes in LV short-axis diameter. Distances between MA sutured horn and PM tips were also measured to assess changes in subvalvular geometry.

Successful placement of transmural bead-sets allowed quantification of 3-dimensional myocardial deformations of the mid-lateral region in 4 sheep. Because a boundary exists between the myocardial wall and the PMs which can be distinguished grossly and is also revealed in muscle fiber angle measurements,\(^22\) thereby rendering homogenous strain theory inappropriate at the PM border,\(^23\) care was taken to avoid the PMs during bead set insertion. For strain analysis, the LV long-axis was defined using the anterior basal marker (4; Figure 1) and the apical marker (1), similar to the LV long-axis originally described by Streeter.\(^24\) This long-axis and the 3 epicardial surface beads define a system of local cardiac coordinates aligned with the circumferential ($X_1$), longitudinal ($X_2$), and radial ($X_3$) axes of the LV lateral wall. Because the local epicardial-tangent plane defines this coordinate system, wall curvature is taken into account. Using a least-squares method, a continuous polynomial position field defines this coordinate system, wall curvature is taken into account. With the circumferential ($X_1$), longitudinal ($X_2$), and radial ($X_3$) axes of the LV lateral wall. Because the local epicardial-tangent plane defines this coordinate system, wall curvature is taken into account. Using a least-squares method, a continuous polynomial position field defines the current position of the beads throughout the cardiac cycle.\(^{14,24}\)

The 3 shear strains ($E_{12}, E_{23}, E_{31}$) represent angle changes between pairs of originally orthogonal coordinate axes. Strains were interpolated along the centroid of the bead columns at 1% increments of wall depth from the epicardium at ED. Echocardiographic measurement at the time of bead insertion demonstrating that the most subendocardial bead was consistently at 90% of wall depth (wall depth averaged 10.1 ± 1 mm, the depth of the deepest beads was 9 ± 1 mm from the epicardial surface) allowed for interpolation (0% to 90%) and extrapolation (90% to 100%) of strains through the entire LV wall. The mean error of this method for transmural continuous strain error suggested by J.C.C., computed in cylindrical coordinates on a thick-walled incompressible cylinder undergoing inflation and stretch, torsional and transverse shear, is 1.02% (range, 0.04% to 3.72% for the 6 tensor components) (K. Kindberg, unpublished data, 2004).

Because strain in the heart is heterogeneous with respect to wall depth, it is necessary to evaluate strain patterns at different depths independently; transmural strains at 20% (subepicardial), 50% (mid), and 80% (subendocardial) wall depth were selected for analysis. Changes in bead positions at ED postcut (deformed configuration) were compared with those from ED at baseline (precut, reference configuration) to assess changes in local transmural myocardial geometry at end-diastole (ie, end-diastolic strain), which describes changes in regional 3-dimensional geometry at ED associated with acute alterations in material properties between precut and postcut. Systolic strains were calculated by comparing bead positions at ES (deformed configuration) with ED (reference configuration) for each data run (3 beats per run) before and after cut. All data are reported as mean ± 1 SD. End-diastolic strains were compared with zero using a 1-sample $t$-test. Changes in hemodynamics, global geometry, and systolic strains at each depth were compared using Student $t$ test for paired observations. The effect of chordal cutting on PRSW as related to the X-intercept of the linear regression ($V_a$) was also assessed using an analysis of covariance (ANCOVA) model. Degree of MR was compared using Wilcoxon signed-rank test for nonparametric observations. The level of significance was taken as $P<0.05$. Not surprisingly, in the 6 animals with damaged first-order chordae, MR increased significantly ($0.8±0.4$ versus $2.5±1.2$; $P=0.03$), underscoring the importance of primary chordae for valvular competence.

### Results

CPB time was 80±9 minutes, and aortic cross-clamp time was 60±7 minutes. Correct marker placement and successful transection of the 2 most medial second-order strut chordae without damage to first-order chordae or AML in these 8 animals was confirmed on necropsy.

Before chordal cutting, traces to mild MR was detected; there was no change in the degree of MR after transection of the strut chordae ($0.4±0.4$ [precut] versus $0.6±0.4$ [postcut]; $P=NS$). Not surprisingly, in the 6 animals with damaged first-order chordae, MR increased significantly ($0.8±0.4$ versus $2.5±1.2$; $P=0.03$), underscoring the importance of primary chordae for valvular competence.

### Systolic Temporal Dynamics and Hemodynamics

After chordal cutting, neither heart rate ($111±16$ versus $107±14$ minutes$^{-1}$; $P=0.14$) nor time from ED to ES ($271±40$ versus and $273±41$ ms, $P=0.76$) changed, but time from ED to mid-ejection was significantly delayed ($125±18$ versus $136±19$ ms, $P=0.01$).

These altered systolic temporal dynamics were associated with global LV dysfunction as determined by load-independent indices (Table 1 and Figure 2). Systolic function, as estimated by the slope of the end-systolic pressure-volume relationship ($E_{es}$), declined $34\%$ after chordal cutting ($1.48±1.12$ versus $0.98±1.30$ mm Hg/mL, $P=0.04$).

### Table 1. Hemodynamics

<table>
<thead>
<tr>
<th>Hemodynamics</th>
<th>Pre-CUT</th>
<th>Post-CUT</th>
<th>$P$</th>
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</thead>
<tbody>
<tr>
<td>Heart Rate (min$^{-1}$)</td>
<td>111±16</td>
<td>107±14</td>
<td>0.14</td>
</tr>
<tr>
<td>LV + dp/dt$_{max}$ (mm Hg/s)</td>
<td>2730±468</td>
<td>2500±364</td>
<td>0.16</td>
</tr>
<tr>
<td>LV EDV (mL)</td>
<td>182±47</td>
<td>184±42</td>
<td>0.44</td>
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<tr>
<td>LV ESV (mL)</td>
<td>132±33</td>
<td>134±31</td>
<td>0.14</td>
</tr>
<tr>
<td>LV EDP (mm Hg)</td>
<td>16±5</td>
<td>13±5</td>
<td>0.21</td>
</tr>
<tr>
<td>LV pressure$_{max}$ (mm Hg)</td>
<td>111±12</td>
<td>106±11</td>
<td>0.19</td>
</tr>
<tr>
<td>PRSW (mm Hg)</td>
<td>69±16</td>
<td>60±15*</td>
<td>0.03</td>
</tr>
<tr>
<td>$E_{es}$ (mm Hg/mL)</td>
<td>1.48±1.12</td>
<td>0.98±1.30*</td>
<td>0.04</td>
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* $P<0.05$ vs pre-CUT, $t$-test for paired observations.
declined by 15% (69 ± 16 versus 60 ± 15 mm Hg, \( P = 0.03 \)); ANCOVA confirmed this significant effect of chordal cutting on PRSW \( (P = 0.03) \). No load-dependent hemodynamic variable changed demonstrably (Table 1).

**Global LV Geometry**

Chordal cutting resulted in small, but significant, alterations in global LV geometry. Base–apex length increased both at ED \( (8.99 ± 0.59 \text{ cm} \text{ versus } 8.96 ± 0.59 \text{ cm}, \ P = 0.04) \) and ES \( (8.67 ± 0.63 \text{ cm} \text{ versus } 8.74 ± 0.61 \text{ cm}, \ P = 0.02) \), demonstrating that second-order chordae are load-bearing structures serving to maintain LV geometry. The LV apex was displaced away from the LFT at ED \( (9.52 ± 0.59 \text{ cm} \text{ versus } 9.62 ± 0.52 \text{ cm}, \ P = 0.02) \), and from both the RFT \( (8.46 ± 0.59 \text{ cm} \text{ versus } 8.63 ± 0.71 \text{ cm}, \ P = 0.07) \) and the saddle horn \( (9.34 ± 0.71 \text{ cm} \text{ versus } 9.50 ± 0.76 \text{ cm}, \ P = 0.02) \) at ES. No changes in the distances between LV apex and the commissures or the lateral annulus were observed. The posterior PM tip was also displaced away from the mitral saddle horn after chordal cutting both at ED \( (4.76 ± 0.41 \text{ cm} \text{ versus } 4.86 ± 0.44 \text{ cm}, \ P = 0.03) \) and ES \( (4.84 ± 0.39 \text{ cm} \text{ versus } 4.96 ± 0.46 \text{ cm}, \ P = 0.03) \); no anterior PM tip displacement occurred. In the LV short-axis, only septal–lateral diameter at the apical level increased after chordal cutting at ED \( (4.80 ± 0.68 \text{ cm} \text{ versus } 4.89 ± 0.57 \text{ cm}, \ P = 0.03) \), consistent with outward displacement of the posterior PM.

**End-Diastolic Strains**

The end-diastolic global LV geometric changes after chordal cutting paralleled alterations in local mid-lateral LV transmural wall deformations, as determined from analysis of the bead set. Table 2 summarizes the transmural end-diastolic strains after chordal cutting. Transection of the second-order chordae resulted in longitudinal shortening \( (E_{22}) \) strain and radial wall-thickening \( (E_{33}) \) strain in the midwall and subendocardium. Longitudinal–radial shear \( (E_{13}) \) in the subepicardium and subendocardium also occurred.

**Systolic Strains**

Consistent with decreased LV systolic function and altered systolic temporal dynamics, changes in LV transmural systolic strains were also seen after chordal cutting (Table 3). Subepicardial and midwall circumferential shortening \( (E_{11}) \) decreased significantly, as did subendocardial circumferential–longitudinal shear \( (E_{12}) \), i.e., myocardial “micro-torsion”). Two components of subendocardial wall thickening also decreased: circumferential–radial shear \( (E_{13}) \) decreased significantly and the reduction in radial strain \( (E_{33}) \) approached statistical significance \( (P = 0.08) \). Subendocardial longitudinal shortening strain \( (E_{22}) \) increased. To illustrate these findings, subendocardial 3-dimensional cardiac strains throughout the cardiac cycle are shown in Figure 3.
Discussion

The principal findings of this experiment were that cutting the anterior mitral leaflet second-order chordae: (1) altered LV chamber long-axis and subvalvular geometry throughout the cardiac cycle; (2) remodeled end-diastolic transmural myocardial architecture in the equatorial lateral LV region; (3) perturbed midlateral LV systolic deformations and transmural LV wall-thickening mechanics, causing decreased subendocardial "micro-torsion" and wall thickening; (4) changed systolic temporal dynamics with delayed ejection; and (5) impaired global LV systolic function with decreased Ees and PRSW. Moreover, we found that cutting the strut chordae in beating hearts was difficult without damaging first-order chordae, even despite intraoperative isolation of the second-order chordae under direct visualization of the subvalvular apparatus in arrested hearts. Because the first-order chordae are critical for valvular competence, this experience indicates that potential catheter-based approaches for chordal cutting in beating hearts could be hazardous.

This current experiment corroborates the notion that second-order chordae are important for valvular–ventricular interaction and thus preservation of LV systolic pump function. Division of the anterior mitral leaflet second-order strut chordae resulted in deterioration of global LV systolic performance, as reflected by the 34% decline in Ees (end-systolic pressure-volume relation–ship slope). Analysis of PRSW (another load-insensitive measure of LV systolic performance that incorporates both systolic and diastolic information) showed that the SW-EDV relation...

Figure 3. Systolic cardiac strains in the LV subendocardium. Left ventricular pressure (LVP; mm Hg) is on the left ordinate (hollow triangles), with normal strains (E_{11}, E_{22}, E_{33}) and shear strains (E_{12}, E_{13}, E_{23}) in the subendocardium (80% wall depth) on the right ordinate (full circles) as a function of percent cardiac cycle from end-diastole (%) on the abscissa. Data are shown at baseline (precut; black symbols) and after transection of the second-order chordae (postcut; gray symbols) as mean±1SEM for 4 animals (3 beats each) with cardiac cycle lengths normalized and adjusted with cubic Hermite interpolation in time using 5 equally spaced time nodes in the cardiac cycle. Dashed line denotes the time of end-systole (ES) when strains were compared. Arrows point to significant changes at ES.

*P<0.05, Student t test for paired observations.
was highly linear (Figure 2b) and decreased after chordal cutting, again reflecting reduced global pump function.29,30

The mechanisms responsible for second-order chordae valvulo-ventricular interaction may be related to their importance in maintaining elliptical LV geometry and enhancing regional LV wall thickening. Our results demonstrate a link between the second-order chordae and LV structure and function, consistent with previously published works. In porcine studies, van Rijk-Zwikker et al25 found that the anterior leaflet strut chordae remain taut during the cardiac cycle, and Lomholt et al26 measured forces on the second-order chordae that were 3-fold higher than those on first-order chordae (0.7 N versus 0.2 N). From a functional viewpoint, these observations suggest that second-order chordae provide important connections between the cardiac endoskeleton (along the fibrous annulus) and the LV free wall.13 Collagen bundles have been identified in the anterior mitral leaflet radiating away from the strut chordae insertion points to the fibrous portion of the MA between the fibrous trigones.9 In the present experiment, cutting the second-order chordae perturbed global LV geometry. Base–apex LV length increased both at ED and ES, and displacement of the LV apex and PPM tip away from the fibrous annulus after chordal cutting supports the role of second-order chordae as important load-bearing structures. The change in apical displacement from the LFT at ED toward the RFT at ES may reflect contraction of the helically oriented myofibers during systole;22,27 this coupled with no change in the distances between the LV apex and the commissures or the lateral annulus caused the MA to “tilt” as the distance from the apex to the fibrous annulus increased. Such annular “tilting” has been linked with narrowing of the aorto-mitral angle after cutting the second-order chordae.28 Further, subvalvular displacement of only the posterior PM reflects the larger load on the second-order chord originating from the posterior PM than from the anterior PM (0.81±0.1 versus 0.52±0.08 N, P<0.01).13

The geometric perturbations accompanying chordal cutting also included local remodeling of the myocardium in the mid-lateral wall between the PMs. Analysis of end-diastolic strains demonstrated subendocardial and midwall elongation (ES3) consistent with global LV base–apex lengthening (Table 2). Radial wall-thickening (ES4 strain) at ED was also observed in the midwall and subendocardium, possibly reflecting local myocardial unloading in this region after chordal cutting. Longitudinal–radial shear (ES5) in the subepicardium and subendocardium may reflect the increased apical LV septal–lateral diameter at ED, which was measured between markers 5 and 11 (located immediately below the transmural bead set) (Figure 1).

These global and local LV geometric changes may underlie the alterations observed in transmural systolic strains, which provide a mechanism for the LV dysfunction and altered systolic temporal dynamics observed after chordal cutting. Subepicardial and midwall circumferential shortening (ES2) decreased significantly, as did subendocardial circumferential–longitudinal shear (ES3, or myocardial “micro-torsion”), reflecting decreased local contractile function.29,30 Subendocardial circumferential–radial shear (ES5), which is a component of wall thickening, also decreased significantly (Table 3 and Figure 3). Subendocardial radial strain (ES4), another component of wall thickening, also tended to decrease and approached significance at end-systole (P=0.08), which can be appreciated in the bottom left panel of Figure 3. The increase in subendocardial longitudinal shortening strain (ES3) may reflect increased preload stretch (increased base–apex length and local longitudinal lengthening at ED) and/or possible local myocardial unloading along the LV long-axis after chordal cutting.

The observations from the present study support earlier work from this laboratory showing regional LV systolic dysfunction at the PM insertion sites after transection of the second-order chordae.13 This previous experiment, however, was unable to detect a significant decline in global LV function (although such a trend was noted), probably because the previous experimental preparation involved a much more complex and longer surgical procedure in which the strut chordae were transected intraproactively and then reapproximated with an interposed strain gauge before “control” data were obtained.12,13 Global hemodynamic data from these earlier experiments comparing “control” and postcut conditions must therefore be interpreted cautiously, because “control” data from these earlier studies were acquired after a very long aortic cross-clamp time and after the second-order chordae had already been cut and reapproximated.12,13 The inability to detect a statistical difference in these earlier studies may also have just represented a type II (or β) statistical error because of the small numbers.31

Conversely, Messas et al did not observe a decline in LV ejection fraction after cutting the second-order chordae.10,11 This may be because ejection fraction is a load-dependent index of LV systolic function and LV volume status was purposefully adjusted in their experiment after intraoperative chordal cutting to restore pre-CPB (and prechordal cutting) cardiac output and LV pressures.10,11 In the present experiment, we used PRSW and Ees (load-independent indexes of global LV systolic function) and the experimental design allowed for paired, sequential comparisons between precut and postcut conditions in the same animals without confounding factors such as a procedure on CPB or preload alterations between study conditions. After chordal cutting, both PRSW and Ees decreased significantly (Table 1), reinforcing the trends observed in our earlier experiment.12,13 A decrease in load-dependent LV +dP/dt max was also observed but failed to reach statistical significance (P=0.16). Although this lack of difference in a load-dependent measure of LV function after chordal cutting is consistent with the findings from Messas et al.,10,11 subtle alterations in loading conditions may have influenced LV dP/dt despite the paired sequential nature of our experimental design.

In this acute sheep experiment, severing the mitral second-order strut chordae caused LV geometric perturbations that were associated with functional changes in the lateral LV region. Transmural deformations and wall-thickening mechanics were altered, and global LV systolic function deteriorated. These findings demonstrate that there is a real price to pay in terms of decreased LV systolic function if the second-order chordae are divided. The clinical question is how big a price are we willing to pay if we sacrifice second-order chordae during valve repair for ischemic MR in hearts that are already impaired?

Study Limitations

These data were obtained in an acute, open-chest setting in normal sheep hearts immediately after a complex surgical
procedure and an episode of acute myocardial ischemia; therefore, caution must be exercised when extrapolating these findings to humans with chronic ischemic heart disease. Because the strut chordae are comparatively thinner in ovine hearts, however, we would anticipate that the importance of the strut chordae might be even more pronounced in humans. In addition, although only acute changes were measured, chronic perturbations of LV geometry after chordal cutting resulting in MR and heart failure in sheep have been described. Another limitation is the transient ischemia induced before the precut condition for the purpose of another analysis. Our experimental design, however, allowed for paired, sequential comparisons between precut and postcut conditions in the same animals without other confounding factors. The decrease in LV systolic function observed after cutting the second-order chordae might actually be more substantial in diseased hearts. We acknowledge, however, that we cannot rule out the possibility that the changes in LV function were caused by collateral damage to the endocardial LV surface from the electrosurgery current or perhaps mechanical “tugging” on the second-order chordae during transection. For this reason, animals that had ventricular fibrillation during the cutting attempt were excluded from analysis. Further, it is also unlikely that progressive deterioration of ventricular function under anesthesia contributed significantly to the observed decrease in PRSW and Ees because postcut data were acquired within 5 minutes of precut data. Finally, our transmural strain analysis was limited by the small sample size, because only 4 of the 8 animals with successful chordal cutting could provide satisfactory analysis of transmural bead strains.

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References

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