Chordal Cutting Does Not Adversely Affect Left Ventricle Contractile Function

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Background—Severing a limited number of second-order chordae to the anterior leaflet can improve ischemic mitral regurgitation (MR). Some concerns have been raised regarding possible influence on regional and global left ventricle (LV) function. We evaluated changes in cardiac function in 5 normal sheep with cutting of pre-instrumented chords in the beating heart to maintain constant load.

Methods and Results—Under cardiopulmonary bypass, wires were placed around the 2 central basal chordae and brought outside the heart, which was restarted. Hemodynamic and imaging data were collected before and after chordal cutting by radiofrequency ablation using those wires. Segmental contractility was assessed invasively using sonomicrometers and noninvasively using Doppler tissue velocity and strain rate (with strain rate viewed as less load-dependent than ejection fraction) at 6 sites: base, mid-ventricle, and apex along the anteroseptal and posterolateral walls. We found no changes from before to after chordal cutting in LV end-diastolic volume (47.2±3.3 after cutting versus 48.4±4.6 mL before cutting, P=0.66), end-systolic volume (21.5±1.2 versus 22.3±2.8 mL, P=0.68), ejection fraction (54.2±1.8 versus 54.2±2.7%, P=0.96), systolic ventricular elastance (7.28±1.68 versus 7.66±2.11 mm Hg/mL, P=0.64), preload-recruitable stroke work (46.6±7.7 versus 50.2±10.7 mm Hg, P=0.76), and LVdP/dt (1480±238 versus 1392±250 mm Hg/s, P=0.45). Doppler tissue velocities and longitudinal strain rates surrounding the papillary muscles were unchanged, as were sonomicrometer longitudinal and mediolateral absolute strains. No wall motion abnormalities were visible around the papillary muscles, and no MR developed.

Conclusion—We find no evidence for acutely decreased global or segmental LV contractility with chordal cutting. This absence of adverse effects is consistent with long-term clinical experience with cutting these chords in valve repair. (Circulation. 2006;114[suppl I]:I-524–I-528.)

Key Words: chordae ● echocardiography ● mitral valve ● regurgitation

Mitral regurgitation (MR) more than doubles risk of late death after myocardial infarction and coronary revascularization. After infarction, leaflet closure is restricted by tethering to displaced papillary muscles (PMs) and is therefore incompletely treated by annular reduction. Severing a limited number of second-order chordae to the anterior leaflet improves ischemic MR by decreasing leaflet tethering and restoring more normal leaflet shape and coaptation (Figure 1).

Chordae tendineae are classified as finer marginal or first-order chordae that position the leaflet tips and prevent prolapse, and thicker basal, second-order, or strut chordae that insert symmetrically near the anterior leaflet base (Figure 2). After infarction, the PMs are displaced laterally, apically and posteriorly, pulling the leaflet into the left ventricle (LV).

Distortion is prominent in the basal anterior leaflet, creating a bend (the “seagull sign”). Cutting these strut chordae can eliminate this bend, improve coaptation, and reduce MR. Meanwhile, the intact marginal chordae prevent prolapse and can, in principle, continue to maintain LV function through chordal continuity. Preliminary human studies seem to confirm efficacy and safety of this technique.

Because chordae normally preserve LV–mitral continuity and function, some concerns have been raised regarding any possible influence of this chordal cutting technique on LV function. We therefore evaluated global and segmental LV function in normal sheep before and immediately after cutting pre-instrumented chords in the closed beating heart, using the technique of Rodriguez et al. This eliminates cardiopulmonary bypass between the pre-cutting and post-
cutting stages to maintain constant hemodynamics. To avoid confounding factors, this maneuver was performed without altering myocardial perfusion (no infarction) or loading conditions. Global and segmental contractility were assessed using 3-dimensional (3D) echocardiography, Doppler tissue velocities and strain rate, and sonomicrometer pressure–volume loops and segmental strain.

Methods
The authors had full access to the data and take full responsibility for their integrity. All authors have read and agree to the manuscript as written.

Surgical Procedure
Five Dorsett hybrid sheep (40 to 50 kg), anesthetized with thiopental (0.5 mL/kg), intubated, and ventilated at 15 mL/kg with 2% isoflurane, and given glycopyrrolate (0.4 mg intravenous) and vancomycin (0.5 grams intravenous) underwent sterile left thoracotomy. Six sonomicrometer crystals were sutured to the epicardium around the base, apex, and mid-LV near the PMs (Figure 3). A 5-F micromanometer-tipped Millar catheter was placed in the LV and oxygen saturation monitored. Femoro-caval cardiopulmonary bypass was instituted with hypothermic cardioplegia; after left atrial incision, the anterior mitral leaflet was everted through the annulus, and the 2 most central basal chordae identified and encircled with metallic wires that were exteriorized through the LV wall. The atrium was closed, the heart rewarmed and defibrillated, and circulation restored.

Before cutting, imaging and hemodynamic and sonomicrometer data were acquired. Radiofrequency current was applied to the wires until the chordae were cut and the wires removed. After a 15-minute recovery period, data acquisitions were repeated. The animals were euthanized and the mitral valve examined to confirm cutting of the correct chordae. Experiments conformed to the Guide for the Care and Use of Animals of the American Physiological Society, with Institutional Review Board approval.

Sonomicrometer Acquisitions
Six sonomicrometer crystals were fixed to the epicardium (apex, anterior base, posterior base, lateral base, mid-ventricle posterior, mid-ventricle anterior) and connected to an ultrasound transceiver (TRX98116; Sonometrics, London, Canada). The LV catheter was connected to an amplifier (PREK98099; Sonometrics). Sonometric data, ECG, and LV pressure were digitized and analyzed using CardioSoft 3.4.24 (Sonometrics). Temporary inferior vena cava occlusion generated pressure–volume loops to evaluate end-systolic elastance (Ees) as a measure of contractility, end-diastolic pressure–volume relationship, preload-recruitable stroke work (PRSW), and maximal LV dp/dt. PRSW was calculated from the stroke work–end-diastolic volume relationship during caval occlusion, and Ees was derived from the slope of the end-systolic pressure–volume relationship. Regional strain was calculated as the (end-diastolic distance)–(end-systolic distance)/(end-systolic distance). Longitudinal strain was measured using the base-to-apex distance (Figure 3, crystals 3 and 6) and side-to-side strains at the base and mid-ventricular levels were measured using crystal pairs 1 to 4 and 2 to 5.

3D Echocardiography
Data were acquired with a 5-MHz epicardial transducer (Phillips Sonos 5500), scanning in long-axis from the LV apex using a rotating array aligned through the center of the mitral valve. Onboard software recorded 30 rotated images automatically every 6°, with ECG gating and suspended ventilation. Digital images were transferred to a Silicon Graphics workstation. LV volumes were obtained using endocardial borders from 9 rotated views and a validated surfacing algorithm. MR stroke volume was calculated as LV ejection volume minus aortic outflow volume directly measured by flowmeter. The least-squares plane of the mitral annulus (hinge points confirmed by cine-loop review) was established as the reference frame for mitral geometry, analyzed at mid-systole (time of closest leaflet-annulus approach).2
Tissue Doppler Velocity

We used the low-pass filter to measure tissue Doppler velocities, with sample volumes placed in the basal, middle, and apical segments of the posterolateral and anteroseptal walls (Figure 4). The Doppler beam was aligned parallel to these walls to assess local longitudinal contraction as peak systolic velocities. Strain rate was calculated as the difference in tissue velocities between segments, base minus mid-ventricle and mid-ventricle minus apex for each wall, divided by the distance between each pair of sample volumes.19

Statistical Analysis

Hemodynamic and echo-Doppler measurements were compared among stages and sheep by 2-tailed paired t tests (pre-cutting versus post-cutting), with significance at \( P<0.01 \) (Bonferroni-corrected) using SPSS 14.0 (SPSS, Chicago, Ill). Tissue Doppler velocities \((n=10)\) measured by 2 independent observers gave a variability of 2.5% of the mean.

Results

Hemodynamics and Global LV Function

No significant change was found before and after chordal cutting in heart rate, LV pressure and cardiac output, and invasive (Ees, PRSW, and \( dP/dt \)) and noninvasive (ventricular volumes and EF) measurements of global LV function (Table 1). The pressure–volume loops did not appreciably change before and after chordal cutting, without significant change in Ees or end-diastolic pressure–volume curve (Figure 5).

<table>
<thead>
<tr>
<th>TABLE 1. Hemodynamic and Global LV Function</th>
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<tr>
<td>Before Cutting</td>
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<td>HR, bpm</td>
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<td>LVP, mm Hg</td>
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<td>LVEDP</td>
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<tr>
<td>LV EDV, mL</td>
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<tr>
<td>LV ESV, mL</td>
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<tr>
<td>EF, %</td>
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<tr>
<td>Ees, mm Hg/mL</td>
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<tr>
<td>PRSW, mm Hg</td>
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<td>LV dp/dt, mm Hg/s</td>
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Ees indicates elastance; EF, ejection fraction; HR, heart rate; LVEDV, LV end-diastolic volume; LVES, LV end-systolic volume; LVP, LV pressure; PRSW, preload-recruitable stroke work.

Regional LV Function (Table 2)

Invasive (absolute strains from sonomicrometry) and noninvasive measures (tissue Doppler velocities and strain rates) of regional LV function did not significantly change before and after chordal cutting, including measurements in PM regions (mid-ventricle, Figure 3: Doppler tissue velocities at the mid-ventricular sites, and strain rates from base to mid-ventricle and mid-ventricle to apex for both anteroseptal and posterolateral walls). No segmental wall motion abnormalities or changes in local LV configuration appeared on echocardiographic images before and after cutting.

Mitral Valve Competence

Prolapse and MR did not develop after chordal cutting in any of the experiments. In one experiment, after delivery of radiofrequency energy, transient elevation of LV end-diastolic pressure and hypotension occurred, resolving completely after 10 minutes.

<table>
<thead>
<tr>
<th>TABLE 2. Invasive and Noninvasive Regional LV Function Evaluation</th>
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<tr>
<td>Before Cutting</td>
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<tr>
<td>Absolute Strain</td>
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<td>Basal transverse strain</td>
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<td>Mid-ventricle transverse strain</td>
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<td>Longitudinal strain</td>
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<td>Doppler Tissue Velocities, cm/s</td>
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<tr>
<td>LAT-apex</td>
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<td>LAT-mid</td>
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<td>LAT-base</td>
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<tr>
<td>IVS-apex</td>
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<td>IVS-mid</td>
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<td>IVS-base</td>
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<tr>
<td>Strain Rate, s(^{-1})</td>
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<tr>
<td>LAT-mid-apex</td>
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<tr>
<td>LAT-base-mid</td>
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<td>IVS-mid-apex</td>
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<td>IVS-base-mid</td>
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Ees indicates interventricular septum; LAT, lateral.
Discussion

Recent studies have demonstrated that severing 2 second-order chordae to the anterior leaflet reduces ischemic MR by relieving restriction of the basal leaflet and improving coaptation. Goetz et al have confirmed that chordal cutting increases leaflet mobility,\(^2\) which can improve coaptation of tethered valves. Chordal cutting has also been of interest for repair of myxomatous valves (transposing chordae to unsupported segments) and rheumatic valves.\(^2\) Because complete chordal transection can reduce LV function, leading to chordal-sparing valve replacement,\(^15\) it was necessary to explore the effects of selective and limited chordal cutting on ventricular function. Our results showed no significant changes after chordal cutting in LV volumes, ejection fraction, dP/dt, or preload-independent measures of global contractility, including Ees and PRSW. Doppler tissue velocities and strain rates were unchanged at all sites, including the mid-ventricle. Sonomicrometer crystals confirmed the absence of changes in segmental strain. No wall motion abnormalities appeared, and no MR developed. Of note, in 1 sheep, application of the radiofrequency current was transiently followed by increased LV end-diastolic pressure, resolving after 10 minutes. This may have been caused by the radiofrequency current itself, because any effect from chordal cutting would likely have been permanent.

Several additional lines of evidence suggest the safety of this procedure. In chordal-sparing valve replacement, only the posterior leaflet and its chordae are most commonly preserved, and EF is typically maintained. For many years, these basal chordae have been disconnected in routine repair of rheumatic and myxomatous valves without adverse effects.\(^2\) In isolated perfused hearts, severing all the basal chordae only slightly decreased shortening of a single myocardial segment.\(^2\) In therapeutic applications, however, only 2 chords are cut, and although they individually bear more stress, Kunzelman and Cochran have suggested that “it may be possible surgically to remove basal chordae without seriously compromising mitral valve function.”\(^10\) In ischemic hearts, if MR can be reduced, the dominant effect of ventricular decompression may be increased contractile function due to reduced wall stress. Relief of ischemic MR without prolapse or decreased LV global function has been confirmed in sheep with acute infero-basal infarction (unchanged LVEF, pressure, and dP/dt).\(^8\) LVEF was also preserved after chordal cutting 2 months after infarction, or by chordal cutting and annuloplasty, MR decreased, without decreased EF.\(^12\) Tirone David and Michael Borger have cut the medial chords to both leaflets in patients with inferior infarctions; preliminary communications to date do not indicate decreased LV function. Yamamoto et al have reported 1 patient with ischemic MR treated by chordal cutting, annuloplasty, and cardiac volume reduction; after 6 months, EF was maintained.\(^13\) Fayad et al reported unchanged EF and decreased MR both at rest and after exercise at 2-year follow-up in a patient treated by chordal cutting alone via aortotomy.\(^13\)

Part of the motivation for this work was to address questions arising from a series of studies on chordal cutting. Initially, Timpek et al showed that severing basal chordae in sheep without infarction (to explore potential use in supporting prolapsing segments) did not alter LV size or function.\(^2\) More recently, the same group reported mild localized changes in regional fractional area shortening in 3 epicardial segments (2 apical). The largest changes were in regional PRSW, a derived value with wide scatter, for which the authors felt it necessary to discard some or all values in 7 of 8 sheep because of unphysiologic results.\(^2\) Global systolic function, systolic and end-diastolic pressures, LV dP/dt, global elastance, and global PRSW were unchanged. In contrast, a further study suggested a decrease in global systolic function.\(^17\) In that work, chordal cutting was preceded by the induction of transient ischemia in the papillary muscle territory.\(^2\) Ingeniously, the chords were cut by radiofrequency ablation in the beating heart using wires looped around them to compare hemodynamics before and after cutting without changes in load. We adopted this approach in the present study but avoided ischemia to remove a potentially confounding variable. The authors reported a mild decrease in global end-systolic elastance (\(P=0.04\)) and decreased PRSW (\(P=0.03\)). However, there were no changes in load-dependent measures, and there were no changes in loading conditions to limit the applicability of these measures, which included LV volumes (and by implication EF and cardiac output), LV pressures, and dP/dt.\(^17\) Interestingly, in the same sheep, PRSW was identical before and after chordal cutting when circumflex-territory ischemia was induced,\(^2\) negating the concern that chordal cutting would be most problematic in the ischemic heart. The authors noted that perhaps the electrocautery itself and the mechanical traction needed to sever the chords in the beating heart could have affected function in subtle ways and so too, could the preceding ischemia.

The current study using a similar radiofrequency approach but without ischemia has shown no acute changes in global function or regional strain measured noninvasively by Doppler or invasively by sonomicrometers. In one instance, electrocautery produced myocardial depression that resolved completely over 10 minutes, consistent with one proposed explanation of the Stanford group for their observed changes, which were measured within 5 minutes of ablation.

Limitations and Future Directions

In this study, to address concerns about potential acute adverse effects, chordal cutting was performed acutely in nonischemic hearts. Further studies are therefore needed to evaluate this technique in the setting of chronic ischemic MR, in which it would be most useful. Nonetheless, this approach allowed us to study the isolated effect of chordal cutting on regional and global LV function without any confounding factors such as ischemia or extracorporeal circulation.
Variable effects may be expected if the same chordae are not consistently cut; therefore, in all animals, the mitral valve was examined to confirm cutting of the 2 central strut chordae.

Although strut chordae in sheep may be thinner than in humans, so are the mitral leaflets, and there is no reason to expect that the physical forces on these structures do not scale accordingly.

The labor-intensive nature of the procedure limited the number of sheep studied. To evaluate the precision for measuring changes as a means of analyzing the power to test hypotheses, 95% confidence intervals were computed for differences in key indices of LV volume and function from before to after chordal cutting. Specifically, based on 95% confidence intervals, the maximal increase in LVEDV is 0.2% of the mean (0.12 mL), the maximal increase in LVESV is 8.9% of the mean, and the maximal decrease in LVEF is 4% of the mean (a decrease of 2.2 in EF itself), even though changes in all of these variables were not significant, with average values in the direction of decreased remodeling. The maximal predicted decrease in mid-ventricular transverse strain is 12.1% of the mean (1.7% strain), and the maximal decrease in mid-ventricle to apex longitudinal strain rate is 2.5% of the mean (1.2%/s strain rate), although on average these measures both increased insignificantly. Therefore, we believe the consistency of the results provides a reasonably precise basis for power to reject the hypothesis that chordal cutting causes important adverse LV remodeling.

Finally, this approach to reduce tethering allows for additional options, including chordal elongation, that would obviate concerns about disconnection.

Conclusion

We found no evidence for acutely decreased global or segmental contractility with chordal cutting performed in the closed heart. This absence of adverse effects is consistent with long-term clinical experience with cutting these chords in valve repair.

Acknowledgments

We thank Dr Marielle Scherrer-Crosbie for her experience and guidance on strain and strain rate measurement, and Dr David J. Dorer for his guidance with the statistical analysis. J. L. Guerrero’s skills were critical to implementing this procedure.

Disclosures

None.

References


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Circulation. 2006;114:I-524-I-528
doi: 10.1161/CIRCULATIONAHA.105.000612

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