Efficacy of Chordal Cutting to Relieve Chronic Persistent Ischemic Mitral Regurgitation

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Background—Mitral regurgitation (MR) conveys adverse prognosis in ischemic heart disease. Leaflet closure is restricted by tethering to displaced papillary muscles, and is, therefore, incompletely treated by annular reduction. In an acute ischemic model, we reduced such MR by cutting a limited number of critically positioned chordae to the leaflet base that most restrict closure but are not required to prevent prolapse. Whether this is effective without prolapse, recurrent MR, or left ventricular (LV) failure in chronic persistent ischemic MR, despite greater LV remodeling, remains to be established. Therefore, we studied 7 sheep with chronic inferobasal infarcts known to produce progressive MR over 2 months. In all of those sheep, after a mean of 4.1 months, the 2 central basal (intermediate) chordae were cut at the chronic ischemic MR stage. 3-Dimensional echo quantified MR, LV function, and valve geometry. Five other sheep were followed for a mean of 7.8±1.2 months after inferobasal infarction with chordal cutting.

Results—All 7 of the sheep with chronic ischemic MR (increased from 1.4±0.4 to 11.2±0.5 mL/beat, regurgitant fraction=39.0±4.2%, P<0.0001) showed anterior leaflet angulation at the basal chord insertion. Although end-systolic volume had doubled, cutting the 2 central basal chordae significantly decreased the MR to baseline (P<0.0001) without prolapse or decline in EF (41.1±1.5% to 42.6±1.6%, P=not significant [NS]). The five sheep with long-term follow-up showed no prolapse or MR, and no significant post-infarct decrease in LV ejection fraction (EF; 38.9±2.4% to 41.4±2.2%, P=NS).

Conclusion—Cutting a minimum number of basal (intermediate) chordae can improve coaptation and reduce chronic persistent ischemic MR without impairing LVEF. No adverse effects were noted long-term after chordal cutting at the time of infarction. (Circulation. 2003;108[suppl II]:II-111-II-115.)

Key Words: mitral valve — regurgitation — remodeling — echocardiography

Ischemic MR is a common complication of ischemic heart disease that conveys adverse prognosis after infarction or revascularization, more than doubling mortality.1,2 It increases wall stress and promotes LV remodeling and dysfunction, which begets more MR.3 Patients with various MR lesions have benefited recently from surgical repair as opposed to replacement, with improved LV function and decreased complications.4 However, the efficacy of repair has been particularly elusive for patients with ischemic MR, in whom decisions regarding repair must often be made during coronary artery revascularization. Extensive evidence from a number of groups has confirmed the relation of ischemic MR to remodeling and distortion of the ischemic LV.5–10 Displacement of the attached papillary muscles (PMs) tethers the leaflets into the LV and restricts their ability to close effectively at the level of the annulus, which may also dilate. Tethering is compounded by contractile dysfunction, decreasing the closure force opposing tethering.11

Therefore, ischemic MR is an imbalance of the entire mitral-ventricular complex, so that reducing annular size alone is often ineffective because of persistent leaflet tethering,12,13 particularly with continued remodeling.14,15 Inconsistent benefits, prolonged bypass and ischemic time, and increased mortality often deter surgical repair. An alternative technique is based on the observation that increased tethering creates an angulated bend in the basal anterior leaflet, limiting its ability to coapt effectively (Figure 1, center).5,16 This leaflet portion is held nearly rigid by basal or intermediate chordae inserting closest to the annulus. The more distal leaflet pivots around this “knee,” but only its tip can then meet the posterior leaflet, decreasing the coaptational surface needed for effective closure.

Therefore, we proposed the hypothesis that cutting a limited number of these critically positioned basal chordae...
cardioplegia; after left atrial incision, the anterior mitral leaflet was instituted with caval and femoral artery cannulation and hypothermic imaging was repeated and the thoracotomy closed.

imaging was performed and the second and third circumflex obtuse the day before infarction. After the pericardium was opened, baseline before infarction, and oral acebutolol (400 mg) and aspirin (250 mg)

mg/kg i.v. followed by 2 mg/min) given 10 minutes before coronary ligation. Sheep received oral amiodarone (1200 mg daily) for 2 days before infarction, and oral acebutolol (400 mg) and aspirin (250 mg)

can improve coaptation and reduce ischemic MR; eliminating the anterior leaflet bend can allow the leaflets to assume a more normal and less taut configuration, with more effective coaptation (Figure 1, right). The intact marginal chordae to the leaflet edges should still prevent prolapse. As an initial approach to alter the minimum number of structures, we cut the 2 basal chordae attached to the central anterior leaflet, which are under greatest tension because of outward PM displacement. These chordae are cut at their valvular insertions. This approach has successfully reduced MR in an acute ischemic model. However, in the clinical perspective, it is important to establish whether chordal cutting remains effective in chronic persistent ischemic MR despite the possibility of greater LV and annular dilatation. Therefore, this was tested in a sheep model of chronic ischemic MR using 3-dimensional and Doppler echocardiography to quantify MR and relate it to 3-dimensional changes in valve configuration.

Methods

The chronic infarction model of Llaneras et al17,18 offers the opportunity to study MR evolution in the same animals with stable infarction. Evaluations are at baseline, with chronic infarction and moderate MR, and after improved coaptation by basal chordal cutting. Seven Dorsett hybrid sheep (40–50 kg), anesthetized with thiopentothal (0.5 mL/kg), intubated and ventilated at 15 mL/kg with 2% isofluorane and oxygen, and given glycopyrrolate (0.4 mg i.v.) and prophylactic vancomycin (0.5 g i.v.), underwent sterile left thoracotomy, with procainamide (15 mg/kg i.v.) and lidocaine (3 mg/kg i.v. followed by 2 mg/min) given 10 minutes before coronary ligation. Sheep received oral amiodarone (1200 mg daily) for 2 days before infarction, and oral acebutolol (400 mg) and aspirin (250 mg) the day before infarction. After the pericardium was opened, baseline imaging was performed and the second and third circumflex obtuse marginal (OM) branches ligated to infarct the interposterior wall. Imaging was repeated and the thoracotomy closed.

After a mean of 4.1±0.5 months, each animal had a second thoracotomy under general anesthesia. Cardiopulmonary bypass was instituted with caval and femoral artery cannulation and hypothermic cardioplegia; after left atrial incision, the anterior mitral leaflet was everted through the annulus, and the 2 most centrally attaching basal chordae cut.16

After repair of the atrial incision, rewarming, and defibrillation, normal circulation was restored, and, if necessary, saline infused to restore pre-bypass cardiac output and LV pressure, with repeat imaging and hemodynamics [left atrial (LA) and LV pressures].

Chronic Follow-Up Evaluation

As an initial step to study the long-term effect of chordal cutting, a separate group of 5 sheep with the same infarction (ligation of OM2 and OM3) were followed for 7.8±1.2 months (up to 11 months). Chordal cutting was performed in this group at the time of acute infarction. 3-Dimensional echo was performed just after acute infarction (before chordal cutting) and at follow-up (chronic infarction with chordal cutting).

3-Dimensional Echocardiography

Thirty rotated LV apical views were acquired (5 MHz epicardial Philips Sonos 5500) with suspended respiration, as described previously, and validated against sonomicrometry.7,19 3-Dimensional LV volumes were obtained using endocardial borders from 9 views.20 MR stroke volume was calculated as LV ejection volume minus aortic outflow volume directly measured by flowmeter.21 The least-squares plane of the mitral annular hinge points was established as reference frame;19 projecting the annulus onto this plane gave mitral annular area (MAA). Mitral geometry was analyzed at mid-systole (time of closest leaflet-annulus approach),5,22 including the PM-to-annulus tethering distance described previously. The 3-dimensional leaflet surface area separating the LA and LV cavities was reconstructed,19 and the leaflet tenting volume measured between the leaflet surface and the least-squares annular plane. The bent anterior leaflet shape (Figure 1, center) was assessed by leaflet orientation (normally concave toward the LV, becoming convex with tenting). Mitral leaflet closing force was calculated as annular area times transmural pressure difference.

Statistical Analysis

Measures were compared among stages and sheep by 2-way ANOVA, explored if significant by 2 paired t-tests (chronic ischemia versus baseline and versus chordal cutting), with significance at P≤0.01 (Bonferroni-corrected). MR stroke volume determinants were explored using univariate and stepwise multiple linear regression analysis, entering geometric and functional measures [tenting volume and MAA, along with LV end-diastolic volume (EDV), LV end-systolic volume (ESV), LVEF and closing force] as suggested by the F value at P<0.05. Tenting volume measurements (n=10) by 2 independent observers gave a variability of 2.5% of the mean.

Results

Progression of Ischemic MR

With acute infarction, LV dilatation was limited, and, as at baseline, the leaflets closed at the annular level with only trace MR. However, after a mean of 4.1 months of infarction, LV volumes were considerably higher (36.6±6% higher end diastolic and 100±1% higher end systolic volumes), with mild bulging of the affected wall and PM tip displacement away from the annulus; the leaflets were apically tented, with moderate MR (regurgitant volume=11.1±0.5 mL/beat, regurgitant fraction=39±4.2%, versus 1.4±0.4 mL/beat at baseline). There was increased tenting volume, and LA pressure increased from 10.5±0.7 to 20±1.7 mmHg (P<0.0001,Table 1, Figures 2 and 3). Figure 3 (lower center

![Image](http://circ.ahajournals.org/)

**Figure 1.** Left, at baseline, leaflet area exceeds that needed to cover the annulus, creating a coapting leaflet surface to prevent MR. Center, inferior infarction most distorts the base of the anterior leaflet, which is tethered by basal chordae to form a bend, reducing the coapting surface and causing MR. Right, basal chordal cutting can eliminate this bend, improve coaptation, and reduce MR; the marginal chordae prevent prolapse.
panel) shows the more globular LV with chronic MR and remodeling.

**Reversal of Ischemic MR**

Cutting the 2 basal chords alleviated the apical tenting and restored MR to baseline (Table 1; Figure 3, right) without prolapse or decreased EF (41.1 ± 1.5% to 42.6 ± 1.6%, \( P = \text{NS} \)). The changes in MR volume paralleled those in tenting volume (Figure 2), with a curvilinear exponential rise of MR with tenting volume (\( r^2 = 0.89 \)). There were no significant changes with chordal cutting in LV pressure, LV volume, or mitral leaflet closing force; LA pressure decreased with relief of MR. Mitral annular area increased with chronic inferior ischemia and the development of MR and a higher LA pressure, and decreased slightly but not significantly with chordal cutting and relief of MR (decreased LA pressure).

<table>
<thead>
<tr>
<th></th>
<th>Baseline (1)</th>
<th>Chronic MI (2)</th>
<th>Chordal Cutting (3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR (bpm)</td>
<td>110 ± 1.3</td>
<td>115 ± 1.9</td>
<td>115 ± 1.7</td>
</tr>
<tr>
<td>LVP (mm Hg)</td>
<td>86 ± 1.7</td>
<td>74.2 ± 1.1*</td>
<td>74.1 ± 1.9</td>
</tr>
<tr>
<td>LAP (mm Hg)</td>
<td>10.5 ± 0.7</td>
<td>20 ± 1.7*†</td>
<td>12.9 ± 0.6†</td>
</tr>
<tr>
<td>LV EDV (ml)</td>
<td>45.7 ± 1.7</td>
<td>62.2 ± 2.05*</td>
<td>62 ± 2.1</td>
</tr>
<tr>
<td>LV ESV (ml)</td>
<td>18.8 ± 1.6</td>
<td>37.7 ± 1.9*</td>
<td>35 ± 1.9</td>
</tr>
<tr>
<td>EF (%)</td>
<td>61.9 ± 1.3</td>
<td>41.1 ± 1.5*</td>
<td>42.6 ± 1.6</td>
</tr>
<tr>
<td>Ao Stroke Volume (ml)</td>
<td>25.4 ± 1.5</td>
<td>13.7 ± 1.2*</td>
<td>25.2 ± 1.1†</td>
</tr>
<tr>
<td>MR Stroke volume (ml)</td>
<td>1.4 ± 0.4</td>
<td>11.1 ± 0.5*</td>
<td>1.4 ± 0.4†</td>
</tr>
<tr>
<td>Tenting volume (cm³)</td>
<td>0.97 ± 0.04</td>
<td>2 ± 0.06*</td>
<td>1.08 ± 0.41†</td>
</tr>
<tr>
<td>Leaflet shape: (concave: 0 convex: 1)</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>MA area (cm²)</td>
<td>5.48 ± 0.15</td>
<td>6.24 ± 0.19*</td>
<td>5.9 ± 0.14</td>
</tr>
<tr>
<td>Closing force (mm Hg/cm²)</td>
<td>418 ± 2.3</td>
<td>357.5 ± 3.5*</td>
<td>355 ± 2.7</td>
</tr>
</tbody>
</table>

LVP: LV pressure. LAP: LA pressure. LVEDV: LV end-diastolic volume. LVESV: LV end-systolic volume. MA: mitral annulus. All 2-way ANOVA but one (heart rate) were significant \( P = 0.01 \). Significant changes \( (P = 0.01, \text{Bonferroni}) \) are indicated for the 2-way comparisons: *baseline vs. chronic MI, †chronic MI vs. chordal cutting.

Univariate predictors of MR stroke volume were tenting volume and MAA but not LV ejection fraction or closing force. Multiple stepwise regression identified tenting volume as the strongest independent determinant of MR stroke volume (\( r = 0.89 \)).

**Long-Term Follow-Up**

The 5 sheep with chordal cutting at the time of inferior infarction showed no prolapse or MR (no more than the normal physiological trace) at long-term follow-up. Unlike sheep without chordal cutting studied at 8 weeks (example in

Figure 2. Changes in MR stroke volume and leaflet tenting volume.

Figure 3. Mid-systolic apical 2-dimensional echo images. Left, normal mitral coaptation at baseline with normal papillary muscle position (top, arrows) and without color Doppler MR (below). Center, mild bulging of the ischemic inferior wall (3 grouped black arrows) with apical leaflet tenting relative to the annulus (dashes) in the direction of tethering (upward arrow). Mild to moderate MR in the more globular remodeled LV is seen below. Right, basal chordal cutting eliminated the anterior leaflet bend (arrow, top) with improved coaptation and no MR (below) despite important LV dilatation. The anterior leaflet convexity toward the left atrium is normal in this view considering the saddle shape of the mitral annulus.\(^{19}\)

Figure 4. Chronic follow-up after inferior MI and chordal cutting–color Doppler apical long-axis views. A, sheep without chordal cutting at 8 weeks: moderate MR accompanies anterior leaflet angulation. B and C, sheep with chordal cutting at 8 weeks and 11 months post-MI, showing no MR and no prolapse.
Discussion

Previous results in vitro and in an acute in vivo model of ischemic MR have shown that tethering and the resulting malcoaptation can be relieved by basal chordal cutting.\(^{16}\) A subsequent logical step is to determine whether chordal cutting is still effective in chronic ischemic MR with greater LV remodeling, and therefore, greater tethering to correct. This study demonstrates that despite LV dilatation with doubled end-systolic volume, cutting the 2 basal chordae corrected the malcoaptation and decreased MR without adverse effects on LV ejection fraction. These chordae normally buttress the anterior leaflet body, but, with PM displacement, they exert a dominant and maladaptive role in distorting the leaflet configuration to limit the effectiveness of coaptation and increase tenting volume and MR.\(^{23}\) Cutting these chordae in a relatively simple manner restores the anterior leaflet toward its normal configuration without a sharp angulation near its base. The leaflet body can then approach the annulus more closely and become concave toward the LV cavity, so that the leaflet tip meets the posterior leaflet more effectively. With less tethering, less leaflet surface area is required to meet the posterior leaflet toward coaptation.\(^{12}\)

Practically, such an intervention aims to overcome the variable, often frustrating results of either isolated coronary revascularization\(^{28}\) or annuloplasty techniques that only incompletely address tethering by modifying the annulus but not the chordal-ventricular leaflet attachments.\(^{12-15}\) Undersizing rings only compensates for the fundamental ventricular tethering problem without correcting it;\(^{28}\) ring insertion also shifts the posterior annulus anteriorly, while the ischemic PM remains posterior, thereby restricting the anterior excursion of the posterior leaflet toward coaptation.\(^{12}\)

A recent editorial suggests that ischemic MR can be difficult to eliminate simply by annular reduction if 1 or both leaflets remain apically tethered.\(^{30}\) Although in experimental studies of acute ischemic MR, antero-posterior annular dimension reduction is helpful,\(^{31,32}\) this is in the absence of the more extensive remodeling and PM displacement, which can develop in the chronic ischemic setting, in which therapeutic decisions regarding valve repair for MR are typically required. This emphasizes the need for the chronic model in the current study.

Limitations and Future Directions

The clinical spectrum of ischemic MR includes varying location and chronicity of ischemia. However, the purpose of this study was specifically to demonstrate that cutting a limited number of basal chordae can, in fact, reduce chronic ischemic MR without producing prolapse or significantly decreasing LV ejection fraction. A similar tethered and angulated mitral leaflet configuration is also observed in patients with MR secondary to more diffuse ischemia or dilated cardiomyopathy,\(^{29}\) in whom eliminating MR has been shown to improve ventricular function, symptomatic status, and survival.\(^{33}\) Therefore, it would be reasonable to pursue future experimental studies of chordal cutting in models of more global LV dysfunction and more severe MR, recognizing that a combined approach addressing both chordae and dilated annulus might be needed.

In the 7 sheep studied with chordal cutting at 8 weeks post-MI, MR was observed under general anesthesia, which can decrease the severity of ischemic MR.\(^{28,34,35}\) However, both the moderate MR and its relief by chordal cutting were observed under identical conditions of general anesthesia, which therefore cannot explain the observed decrease. The chordal cutting procedure was brief, with a mean bypass of 15 minutes, and all of the sheep recovered without need for inotropic support. LV volumes, heart rate, and LV closing force were comparable before and after the procedure (Table 1, columns 2 and 3); therefore, the relief of MR cannot readily be attributed to inotropy or volume underloading. The 5 sheep with long-term survival confirm benefit long after the operative procedure.

Despite concerns about the potential for decreased LV function\(^{26,27}\) and increased chordal stresses with chordal cutting, several lines of evidence suggest the safety of this procedure. First, for many years, these basal chordae have been disconnected in routine repair of rheumatic and myxomatous valves without adverse effect.\(^{36,37}\) Second, Timek et al have shown that severing these 2 basal chordae in sheep without MI (to explore potential use in buttressing prolapsing segments) did not cause prolapse or alter the 3-dimensional shape of the valve or its motion; LV size and global function were not significantly changed.\(^{38}\) In isolated perfused hearts, even severing all of the basal chordae, while slightly decreasing shortening of a single segment, did not cause prolapse.\(^{39}\) Third, only 2 chordae are cut, leaving the valvulo-ventricular continuity largely intact. Also, decreasing the MR can potentially diminish the stimulus to remodel,\(^{3}\) and limit progressive increases in wall stress and decreases in LV function. Fourth, based on theoretical considerations, the large number of remaining chordae suggests that individual chordal tension will not measurably increase. Kunzelman and Cochran have noted that the stress borne by marginal chordae exceeds that carried by the basal ones for any strain, with almost twice as many marginal as basal chordal insertions; they suggested that “it may be possible surgically to remove basal chordae without seriously compromising mitral valve function.”\(^{40}\) Furthermore, chordal tension may in fact decrease as, over time, diminished MR stabilizes or reduces LV volume, and the leaflets assume a more normal, less taut configuration (decreased leaflet radius of curvature decreasing tension by Laplace’s Law). In a smaller LV, total stress may be less, even if a greater proportion must be borne by other chords. Fifth, this lack of adverse effect has been the case in the 5 additional sheep studied for a mean of 7.8 months after infarction with chordal cutting, with no prolapse or post-MI...
We thank Shirley Sims for her editorial contributions.

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