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 11.1±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±1.2%, 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 contractional 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...
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 al 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 Dorset hybrid sheep (40–50 kg), anesthetized with thiopental (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 inferoposterior wall. Evaluations are at baseline, with chronic 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 inferoposterior 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.

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. 3-Dimensional LV volumes were obtained using endocardial borders from 9 views. MR stroke volume was calculated as LV ejection volume minus aortic outflow volume directly measured by flowmeter. The least-squares plane of the mitral annular hinge points was established as reference frame; projecting the annulus onto this plane gave mitral annular area (MAA). Mitral geometry was analyzed at mid-systole (time of closest leaflet-annulus approach), including the PM-to-annulus tethering distance described previously. The 3-dimensional leaflet surface area separating the LA and LV cavities was reconstructed, 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 transmirtal 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
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=NS). The changes in MR volume paralleled those in tenting volume (Figure 2), with a curvilinear exponential rise of MR with tenting volume (r²=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).

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 (r²=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 4).
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prevent MR, so that the normal surplus of leaflet area
With less tethering, less leaflet surface area is required to
more closely and become concave toward the LV cavity, so
near its base. The leaflet body can then approach the annulus

38
1.6 mL and an LVEDV of 62.8
1.2 mL, there was no
significant decrease in LVEF (38.9±2.4% to 41.4±1.2%, P=NS).

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 ad-
verse 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
prevent MR, so that the normal surplus of leaflet area
becomes available again to form a coaptational seal.24,25
Meanwhile, the intact marginal chordae continue to prevent
leaflet prolapse or flail, and can in principle continue to
maintain LV function through chordal continuity.26,27

Practically, such an intervention aims to overcome the
variable, often frustrating results of either isolated coronary
revascularization28 or annuloplasty techniques that only in-
completely address tethering by modifying the annulus but
not the chordal-ventricular leaflet attachments.12–15 Undersiz-
ing rings only compensates for the fundamental ventricular
tethering problem without correcting it;29 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 di-

dension 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 re-
quired. 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, recognize-
ing 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 oper-
ative procedure.

Despite concerns about the potential for decreased LV
function26,27 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 myxo-
matus 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 poten-
tially diminish the stimulus to remodel,40 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
decline in LV ejection fraction. Additional survival studies seem indicated with more detailed evaluation of load-independent measures of global and segmental LV function.

Summary
Ischemic MR typically results when leaflet motion is restricted by tethering to displaced papillary muscles, and is therefore incompletely treated by annular reduction. Cutting a minimum number of basal (intermediate) chordae can improve coaptation and reduce chronic persistent ischemic MR even in the remodeled ventricle. It does so without impairing mitral valve function or reducing global LV ejection fraction.

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