Annular or subvalvular approach to chronic ischemic mitral regurgitation?

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Objective: We sought to investigate whether annular or subvalvular interventions corrected chronic ischemic mitral regurgitation differently.

Methods: Sheep underwent placement of markers on the left ventricle, mitral annulus, papillary muscles (anterior and posterior), and both leaflet edges. A transannular suture (septal-lateral annular cinching) was anchored to the midseptal mitral annulus and externalized through the midlateral mitral annulus. Another suture (papillary muscle repositioning) from the posterior papillary muscle was passed through the mitral annulus near the posterior commissure and externalized. After 7 days, 3-dimensional marker data were obtained before inducing posterolateral myocardial infarction. After 7 weeks, animals in whom chronic ischemic mitral regurgitation developed ($n = 10$) were restudied before and after pulling septal-lateral annular cinching or papillary muscle repositioning sutures. End-systolic septal-lateral annular diameter and 3-dimensional displacement of the papillary muscles and leaflet edges were computed.

Results: Infarction increased mitral regurgitation (0.6 ± 0.5 to 2.3 ± 1.1); mitral annular septal-lateral dilation (4 ± 1 mm); posterior papillary muscle displacement laterally (4 ± 2 mm), posteriorly (9 ± 3 mm), and toward the annulus (2 ± 1 mm); posterior mitral leaflet apical tethering (3 ± 1 mm); and interleaflet separation ($+3 \pm 1$ mm, $P < .05$ baseline vs chronic ischemic mitral regurgitation). Septal-lateral annular cinching reduced septal-lateral dimension (-9 ± 3 mm), corrected lateral posterior papillary muscle displacement (4 ± 1 mm) and septal-lateral interleaflet separation (-4 ± 2 mm), and decreased mitral regurgitation (0.6 ± 0.6 , $P < .05$ septal-lateral annular cinching vs chronic ischemic mitral regurgitation) without affecting posterior leaflet restriction. Papillary muscle repositioning reduced septal-lateral diameter (-4 ± 1 mm), moved the anterior papillary muscle closer to the annulus (2 ± 1 mm), and relieved posterior leaflet apical restriction (2 ± 1 mm, $P < .05$ papillary muscle repositioning vs chronic ischemic mitral regurgitation) but did not change lateral posterior papillary muscle displacement or decrease mitral regurgitation (1.9 ± 1.2).

Conclusions: Septal-lateral annular cinching moved the lateral annulus and the posterior papillary muscle closer to the septum and reduced mitral regurgitation unlike posterior papillary muscle repositioning, and thus the key mitral subvalvular repair component must correct posterior papillary muscle lateral displacement.

Despite better understanding of the mechanisms of leaflet malcoaptation in chronic ischemic mitral regurgitation (CIMR), outcomes after valve repair remain poor, and recurrent mitral regurgitation (MR) is seen in upward of 30% of patients within 1 year.¹⁻³ Recent clinical and experimental

Figure 1. A, Schematic of SLAC suture. A 2-0 polypropylene suture was anchored to the midseptal annulus and exteriorized through the lateral annulus to an adjustable tourniquet. S-L, Septal-lateral annular dimension. B, Schematic of PAP suture. A 2-0 polypropylene suture was anchored to the posterior papillary muscle, brought through the mitral annulus near the posterior commissure, and exteriorized to an adjustable tourniquet.

studies show that CIMR results from both interleaflet separation (Carpentier type I) and apical leaflet systolic restriction (Carpentier type IIb).^{4,5} Most surgical methods for CIMR correct annular dilation, such as undersized ring annuloplasty⁶ and septal-lateral annular cinching (SLAC).^{7,8} Other novel procedures, including infarct plication⁹ and papillary muscle sling,¹⁰ normalize posterior papillary muscle displacement (increased tethering distance) to relieve apical restriction. Currently, it is unclear which approach, annular or subvalvular, is superior. To determine which geometric distortions associated with CIMR are most effective in restoring normal leaflet coaptation, we developed a model of CIMR with reversible interventions that could independently manipulate annular and subvalvular geometry: SLAC and papillary muscle repositioning (PAP). We hypothesized that these interventions, designed to correct septal-lateral interleaflet separation and apical leaflet restriction, respectively, would have different effects on mitral geometry and MR.

Methods

Surgical Preparation

Twenty-six Dorsett hybrid sheep (71 ± 5 kg) were premedicated with ketamine (25 mg/kg administered intramuscularly), and anesthesia was induced with sodium thiopental (6.8 mg/kg administered intravenously) and maintained with inhalational

isoflurane (1%-2.5%). Through a left thoracotomy, 8 tantalum myocardial markers (Nos. 13-20, Figure 1) were inserted in the left ventricular (LV) epicardial layer along 4 equally spaced longitudinal meridians, with one marker at the LV apex (No. 12, Figure E1). Polypropylene 2-0 sutures were passed around the second and third obtuse marginal branches of the left circumflex coronary artery.¹¹ On cardiopulmonary bypass, 8 tantalum markers were sutured around the circumference of the mitral annulus (Nos. 0-7) and placed on the anterior and posterior papillary muscle tips (Nos. 10-11) and both mitral leaflet edges (Nos. 8-9).

The SLAC suture was placed by anchoring a 2-0 polypropylene suture to the midseptal annulus (annular saddle horn) and through the midlateral annulus to an external tourniquet (Figure 1, A). The PAP suture was a 2-0 polypropylene suture from the posterior papillary muscle to the annulus near the posterior commissure (Figure 1, B), similar to that described by Kron and colleagues,¹² as an adjunct to ring annuloplasty.

A micromanometer pressure transducer (PA4.5-X6; Konigsberg Instruments, Inc, Pasadena, Calif) was placed in the LV chamber. The coronary artery and SLAC and PAP tourniquets were buried subcutaneously. Four animals died postoperatively.

Experimental Protocol

After 8 ± 2 days, the animals were taken to the cardiac catheterization laboratory, sedated with ketamine ($1-4 \text{ mg} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$, intravenous infusion) and diazepam (5 mg administered intravenously), intubated, mechanically ventilated, and maintained with

inhalational isoflurane (1% to 2.5%). Transesophageal echocardiography (TEE) and coronary angiography were performed, and baseline biplane videofluoroscopic marker and hemodynamic data were acquired (baseline). After premedication with lidocaine (100 mg administered intravenously), bretylium (75 mg administered intravenously), and magnesium sulfate (3 g administered intravenously), the coronary artery snares were tightened to create posteroinferior myocardial infarction. Complete occlusion of the selected vessels was verified by means of angiography. An epinephrine drip was titrated to maintain coronary perfusion pressures (aortic diastolic pressure minus LV diastolic pressure) of greater than 60 mm Hg. Nine sheep died after coronary occlusion from ventricular fibrillation. The surviving sheep were followed for signs of heart failure, and serial transthoracic echocardiography was performed to detect LV dilatation and MR. Of the 13 remaining animals, 3 had only trace-mild MR after 7 weeks. The 10 animals that had significant CIMR (mean, 2.3 ± 1.1) comprised the study group.

After 7 ± 1 weeks, the animals returned to the cardiac catheterization laboratory for TEE and recording of hemodynamic and marker data under control conditions (CIMR) and after reversibly tightening the SLAC suture by 8 to 12 mm (SLAC; Figure 1, A), releasing the SLAC suture, and then tightening the PAP suture by 2 to 6 mm (PAP; Figure 1, B). The MR was graded on the basis of TEE color Doppler regurgitant jet extent and width qualitatively (0-4+) by using parameters described by Helmcke and associates.¹³

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 (Department of Health, Education, and Welfare National Institutes of Health publication No. 85-23, revised 1985). This study was approved by the Stanford University Medical School Laboratory Research Animal Review Committee and conducted according to Stanford University policy.

Data Acquisition

Images were acquired with the animal in the right lateral decubitus position by using a biplane videofluoroscopy system (Philips Medical Systems, Pleasanton, Calif). Data from 2 radiographic views were digitized and merged to yield 3-dimensional (3-D) coordinates for each of the radiopaque markers every 16.7 ms with custom software. Ascending aortic pressure, LV pressure, and electrocardiographic voltage signals were recorded simultaneously during marker image acquisition.

Data Analysis

Hemodynamics and cardiac cycle. Timing Variables from 3 consecutive end-expiratory steady-state beats before infarction were averaged and defined as baseline data for each animal. Similarly, 3 beats at the follow-up study before and after cinching the SLAC and PAP sutures were averaged and termed CIMR, SLAC, and PAP, respectively. End systole was defined at the time of the videofluoroscopic frame containing the point of peak negative rate of LV pressure decrease ($-dp/dt$), and end diastole was defined as the videofluoroscopic frame before the upstroke of the

LV pressure curve. Instantaneous LV volume for each frame (ie, every 16.7 ms) was calculated from the positions of the epicardial LV and annular markers by using a space-filling multiple tetrahedral volume method. This method includes myocardial volume, but changes in this volume accurately reflect changes in chamber size.¹⁴

Papillary muscle geometry. End-systolic papillary muscle positions were determined by using a coordinate reference system (Figure E1) defined by the least-squares best-fit plane of the annular markers, with the origin at the projection of the midseptal annulus marker (No. 0; fibrosa, saddle horn) on this plane, the positive lateral axis in the annular plane passing through the midlateral annulus marker (No. 4), the positive posterior axis in the annular plane directed toward the right fibrous trigone, and the positive apical axis normal to the annular plane and directed toward the LV apex. The end-systolic papillary tip displacements from the midseptal annulus were resolved into their lateral, posterior, and apical components. The saddle horn was chosen as the origin because it is a stable reference (fibrous cardiac skeleton) and a well-defined echocardiographic landmark. The origin of the coordinate system can be moved along the septal-lateral axis to the midlateral (or mural) annulus to see the displacements of the papillary muscles relative to the lateral annulus. If the origin is translated along the lateral axis, the apical and posterior coordinates do not change. Because displacement of the anterior papillary muscle away from the lateral annulus is a potential mechanism for leaflet restriction, lateral displacement of the anterior papillary muscle from the midlateral annulus was also measured.

Mitral leaflet geometry. Apical leaflet restriction was calculated as the end-systolic orthogonal distance from each mitral leaflet edge to the annular plane. The septal-lateral distance between the leaflet edge markers was computed.

Mitral annular geometry. The septal-lateral diameter of the annulus was calculated as the 3-D distance between the markers at the middle of the septal and lateral mitral annulus, respectively (Nos. 0 and 4).

Statistical analysis. All data are reported as means $\pm$ 1 standard deviation. By using repeated-measures analysis of variance with the Dunnett test for multiple comparisons, baseline hemodynamic and geometric data were compared with CIMR data, and SLAC and PAP data were compared with CIMR data to determine the effects of the interventions.

Results

Table 1 summarizes hemodynamic data for baseline, CIMR, SLAC, and PAP conditions. CIMR was associated with more MR (2.2 ± 1.0 ; range, 1.5-4+) than baseline (0.6 ± 0.5 ; range, 0-1+). SLAC returned MR to baseline levels (0.6 ± 0.6 ; range, 0-1.5+), but PAP did not (1.9 ± 1.2 ; range, 1-4+). CIMR decreased dp/dt , whereas SLAC and PAP did not change dp/dt . End-diastolic volume (EDV) and end-systolic volume (ESV) increased from baseline with CIMR; SLAC and PAP did not affect EDV, ESV, heart rate, or LV end-diastolic pressure.

SLAC was associated with a small but consistent increase in LV dp/dt , as well as reduction in ESV and EDV. These differences indirectly reflect improved LV systolic

TABLE 1Hemodynamics

	Baseline	CIMR	SLAC	PAP
MR (0-4+)	0.6 ± 0.5*	2.3 ± 1.1	0.6 ± 0.6*	1.9 ± 1.2
HR (min ⁻¹)	95 ± 15	90 ± 11	89 ± 13	92 ± 15
dP/dt _{max} (mm Hg/s)	1725 ± 623*	1179 ± 508	1419 ± 359	1251 ± 464
LVEDP (mm Hg)	17 ± 4	21 ± 4	19 ± 2	21 ± 3
EDV (mL)	137 ± 25*	169 ± 30	162 ± 31	168 ± 35
ESV (mL)	106 ± 20*	130 ± 21	126 ± 21	130 ± 25

CIMR, Chronic ischemic mitral regurgitation; SLAC, septal-lateral annular cinching; PAP, papillary muscle repositioning; MR, mitral regurgitation; HR, heart rate; dP/dt, maximum time derivative of left ventricular pressure; LVEDP, left ventricular end-diastolic pressure; EDV, left ventricular end-diastolic volume; ESV, left ventricular end-systolic volume. **P* < .05 versus CIMR, repeated-measures analysis of variance and the Dunnett test.

function but did not reach statistical significance by using repeated-measures analysis of variance and correction for multiple comparisons. This possibly could also be due to a type II error given the small sample size.

Table 2 and Figures 2 to 4 summarize end-systolic geometries of the annular and subvalvular components of the mitral apparatus. Annular septal-lateral diameter increased 8 weeks after myocardial infarction (CIMR). SLAC reduced annular septal-lateral diameter relative to CIMR to less than baseline levels, and PAP reduced it to a lesser extent.

CIMR was associated with displacement of the posterior papillary muscle laterally, posteriorly, and closer to the annular plane. SLAC returned posterior papillary muscle position to the baseline position along the septal-lateral axis but did not affect posterior or apical posterior papillary muscle position. PAP moved the posterior papillary muscle even closer to the annular plane but did not alter lateral or posterior displacement of the posterior papillary muscle. Anterior papillary muscle position was not significantly affected by CIMR, SLAC, or PAP. End-systolic lateral displacement of the anterior papillary muscle from the mid-

lateral annulus (0.5 ± 0.5 cm, baseline) was not significantly affected by CIMR (0.7 ± 0.7 cm), SLAC (0.2 ± 0.7 cm), or PAP (0.5 ± 0.6 cm).

CIMR was associated with apical displacement of the posterior mitral leaflet edge at end systole (Carpentier type IIb restricted leaflet motion). SLAC had no effect on posterior leaflet apical restriction, but PAP relieved apical displacement of the posterior leaflet, bringing the leaflet closer to the annular plane. MR caused by annular dilatation (Carpentier type I leaflet motion) was reflected by means of interleaflet separation along the septal-lateral axis. CIMR increased septal-lateral interleaflet separation, which was corrected with SLAC but unchanged by PAP.

Discussion

These experimental findings support the following conclusions: (1) correction of type I interleaflet separation is sufficient to restore mitral competence; (2) correction of type IIb leaflet restriction is neither necessary nor alone is sufficient correct CIMR; (3) lateral displacement of the posterior papillary muscle plays a role in the pathogenesis

TABLE 2Geometric changes in the mitral valvular-ventricular complex

	Baseline	CIMR	SLAC	PAP
Annular S-L (cm)	2.8 ± 0.2*	3.2 ± 0.4	2.3 ± 0.2*	2.8 ± 0.3*
PPM lateral (cm)	3.0 ± 0.3*	3.4 ± 0.3	3.0 ± 0.5*	3.2 ± 0.3
PPM apical (cm)	3.6 ± 0.4*	3.4 ± 0.5	3.4 ± 0.5	3.2 ± 0.5*
PPM posterior (cm)	0.8 ± 0.6*	1.7 ± 0.4	1.7 ± 0.3	1.6 ± 0.4
APM lateral (cm)	2.3 ± 0.4	2.5 ± 0.4	2.2 ± 0.6	2.3 ± 0.5
APM apical (cm)	3.7 ± 0.5	3.7 ± 0.4	3.7 ± 0.4	3.7 ± 0.4
APM posterior (cm)	-1.4 ± 0.6	-1.4 ± 0.6	-1.4 ± 0.5	-1.4 ± 0.6
PML apical (cm)	0.5 ± 0.3*	0.8 ± 0.2	0.8 ± 0.2	0.6 ± 0.2*
AML apical (cm)	0.6 ± 0.4	0.7 ± 0.3	0.6 ± 0.2	0.6 ± 0.3
S-L leaflet separation (cm)	0.6 ± 0.4*	0.9 ± 0.5	0.5 ± 0.4*	0.7 ± 0.4

CIMR, Chronic ischemic mitral regurgitation; SLAC, septal-lateral annular cinching; PAP, papillary muscle repositioning; annular S-L, septal-lateral annular diameter; PPM lateral, distance from the midseptal annulus to the tip of the posterior papillary muscle along the septal-lateral axis; PPM apical, distance from the midseptal annulus to the tip of the posterior papillary muscle along the apical-basal axis; PPM posterior, distance from the midseptal annulus to the tip of the posterior papillary muscle along the anterior-posterior axis; APM, anterior papillary muscle; PML apical, orthogonal distance from the posterior mitral leaflet edge to the annular plane; AML, anterior mitral leaflet; S-L leaflet separation, distance between mitral leaflet edge markers along the septal-lateral axis. **P* < .05 versus CIMR, repeated-measures analysis of variance and the Dunnett test.

Figure 2. Displacements of valvular-ventricular complex between baseline (*left*) and 8 weeks after inferior myocardial infarction (CIMR, *right*). Arrows indicate significant changes ($P < .05$, CIMR vs baseline, repeated-measures analysis of variance with the Dunnett test) in end-systolic septal-lateral annular dimension, papillary muscle displacement, leaflet displacement, and septal-lateral interleaflet separation. CIMR resulted in increased interleaflet separation (type I leaflet motion) and apical restriction of the posterior leaflet (type IIIb leaflet motion) in association with both annular dilation and displacement of the posterior papillary muscle laterally, posteriorly, and toward the base. P, Positive posterior axis; L, positive lateral axis; A, positive apical axis; APM, anterior papillary muscle; PPM, posterior papillary muscle; AML, anterior mitral leaflet; PML, posterior mitral leaflet.

of type I interleaflet separation; and (4) both annular (increased septal-lateral dimension) and subvalvular (lateral displacement of the posterior papillary muscle) geometric distortions should be addressed in the surgical treatment of CIMR during mitral valve repair.

CIMR presents a frustrating clinical problem marked by poor patient survival and recurrence of MR postoperatively.^{1,15} Although there is evidence that correcting CIMR at the time of myocardial revascularization benefits some patients, the question of how best to repair the valve remains unanswered.^{6,16} Some methods, such as undersized ring annuloplasty, focus on correcting annular dilation and type I leaflet malcoaptation. Other procedures are directed toward normalizing apical leaflet restriction (type IIIb leaflet motion) by altering papillary muscle geometry.^{9,10,17} Improved understanding of the relevance of the various geometric perturbations (and mechanisms of leaflet malcoaptation) in CIMR might guide design of more effective surgical interventions. We therefore attempted to manipulate the annular and subvalvular components of the perturbed mitral valve geometry independently in this ovine model of CIMR to assess the significance of such manipulations.

Geometric Changes Between Baseline and CIMR

Seven weeks after inferior myocardial infarction, the mitral apparatus of animals with CIMR had several abnormalities compared with baseline geometry (Table 2 and Figure 3). Annular septal-lateral diameter increased; the posterior papillary muscle was displaced laterally, posteriorly, and toward the annular plane; and the posterior mitral leaflet edge moved away from the anterior mitral leaflet edge in the septal lateral direction (type I leaflet motion) and closer to the LV apex (type IIIb leaflet motion). These findings support and expand on previous clinical findings by using 2-dimensional echocardiography in patients with CIMR.¹⁸ In the study by Yiu and coworkers,¹⁸ displacement of the papillary muscles toward the clinically termed posterior annulus (which is the lateral annulus in the 3-D coordinate system used in this study) correlated better with the development of CIMR than did displacement in the direction of the posterior commissure (called “lateral displacement” in the Yiu study or “posterior” in our 3-D system). Echocardiographic apical displacement, measured as the distance between the fibrosa (mitral annular saddlehorn) and the papillary muscle tip in the 2-dimensional parasternal long-axis view, increased in the Yiu study and correlated with the degree

Figure 3. Displacements of valvular-ventricular complex after tightening SLAC suture. *Arrows indicate significant changes ($P < .05$, CIMR [left] vs SLAC [right], repeated-measures analysis of variance with the Dunnett test) in end-systolic septal-lateral annular dimension, papillary muscle displacement, leaflet displacement, and septal-lateral interleaflet separation. SLAC undersized annular septal-lateral diameter, corrected lateral displacement of the posterior papillary muscle, and reduced septal-lateral interleaflet separation. P, Positive posterior axis; L, positive lateral axis; A, positive apical axis; APM, anterior papillary muscle; PPM, posterior papillary muscle; AML, anterior mitral leaflet; PML, posterior mitral leaflet.*

of CIMR. We have previously reported that the 3-D measured fibrosa-to-papillary-muscle tip distance increases in sheep that experience CIMR as a result of lateral and posterior displacement of the posterior papillary muscle. If apical displacement is defined perpendicular to the annular plane as in our current 3-D study, the posterior papillary muscle moved slightly closer to the annular plane. Thus these 3-D data corroborate previous findings and aid our understanding of the complex geometry of the subvalvular apparatus in CIMR. Previous clinical^{18,19} and experimental^{5,9,20-22} studies of CIMR have demonstrated geometric perturbations at both the annular and subvalvular levels, leading to leaflet malcoaptation with both type I and type IIIb leaflet motion, underscoring the question of which alterations are most important in restoring leaflet coaptation and valvular competency. Displacement of the anterior papillary muscle tip from the lateral annulus has been implicated as a mechanism for leaflet restriction in acute ischemic MR,²³ but in this study of CIMR, lateral, posterior, and apical displacement from the anterior papillary muscle to the lateral annulus did not change between baseline and CIMR.

Geometric Changes With SLAC

Tightening the SLAC suture induced many geometric changes in the mitral valve compared with CIMR (Table 2

and Figure 4). Septal-lateral annular diameter decreased by 9 mm; interestingly, MR was not minimized until the septal-lateral annular diameter was reduced to 5 mm less than the baseline level. This overcorrection of annular septal-lateral dimension was associated with drawing the posterior papillary muscle closer to the septum, thereby normalizing the lateral displacement of the posterior papillary muscle without affecting its apical or posterior displacement. Thus although the apical restriction of the posterior leaflet was unaffected, septal-lateral interleaflet separation was reduced, thereby restoring valve competence.

An important feature of SLAC, originally conceived as an isolated annular intervention,⁷ is this simultaneous correction of lateral displacement of the posterior papillary muscle. Because the septal-lateral diameter of the annulus was overcorrected to less than baseline levels, the posterior papillary muscle moved toward the septum through the connections to the annulus (eg, the chordae tendineae and the lateral wall of the left ventricle). This finding supports the theory proposed by Dagum and associates²³ that the geometries of the annulus and the subvalvular apparatus are tightly coupled, and procedures that remodel annular geometry enough will affect subvalvular geometry. Undersized

Figure 4. Displacements of valvular-ventricular complex after tightening PAP suture. *Arrows indicate significant changes ($P < .05$, CIMR [left] vs PAP [right], repeated-measures analysis of variance with the Dunnett test) in end-systolic septal-lateral annular dimension, papillary muscle displacement, leaflet displacement, and septal-lateral interleaflet separation. PAP reduced septal-lateral annular diameter, moved the posterior papillary muscle closer to the annulus, and corrected apical restriction of the posterior leaflet (but did not affect the degree of MR). P, Positive posterior axis; L, positive lateral axis; A, positive apical axis; APM, anterior papillary muscle; PPM, posterior papillary muscle; AML, anterior mitral leaflet; PML, posterior mitral leaflet.*

ring annuloplasty has been shown to normalize perturbed papillary muscle tethering distances in an ovine model of acute ischemic MR,²⁴ but the present study confirms that undersizing the septal-lateral annular dimension can simultaneously correct lateral displacement of the posterior papillary muscle in CIMR, which is associated with greater magnitudes of abnormal subvalvular geometry.

By bringing the lateral annulus and posterior papillary muscle closer to the septum along the septal-lateral axis, the posterior mitral leaflet edge was also drawn toward the septum, correcting type I interleaflet separation along this axis and decreasing MR. Correction of apical restriction of the posterior leaflet was not necessary to restore mitral competence. This is not surprising because the posterior leaflet is typically restricted after successful ring annuloplasty.²⁵ As a corollary, correction of posterior displacement of the posterior papillary muscle was not necessary to reduce MR.

Geometric Changes With Papillary Muscle Repositioning

Tightening the PAP stitch successfully moved the posterior papillary muscle closer to the annulus and relieved apical restriction of the posterior mitral leaflet (Table 2).

Annular septal-lateral diameter was also reduced but not to the same degree as with SLAC. CIMR, however, was not improved. Why not? CIMR in this model was associated with both apical leaflet restriction (type IIb leaflet motion) and septal-lateral interleaflet separation (type I leaflet motion); although pulling the posterior papillary muscle closer to the annulus corrected the type IIb mechanism of malcoaptation, PAP had no effect on the type I leaflet separation. The position of the posterior leaflet edge is governed by its attachments to the lateral annulus and the papillary muscles, and hence as the annulus dilates in the septal-lateral dimension and the posterior papillary muscle moves laterally in CIMR, the leaflet is drawn laterally (away from the anterior leaflet edge). PAP reduced septal-lateral annular dimension but without decreasing the lateral displacement of the posterior papillary muscle, which explains why it did not affect septal-lateral interleaflet coaptation or the degree of MR.

Comparison of PAP With SLAC

In contrast to SLAC, PAP is an isolated subvalvular intervention that also affected annular geometry, further rein-

forcing the validity of the notion of functional and geometric coupling of the mitral apparatus.²³ SLAC reduced both annular septal-lateral diameter and lateral displacement of the posterior papillary muscle, thus correcting septal-lateral interleaflet separation. PAP reduced annular septal-lateral diameter but did not change the abnormal lateral papillary muscle position and thus did not affect interleaflet separation. These observations suggest that subvalvular geometric distortions, specifically lateral displacement of the posterior papillary muscle, play a role not only in apical leaflet restriction but also interleaflet separation along the septal lateral axis. Although SLAC demonstrated that correction of apical leaflet restriction is not necessary to decrease MR as long as adequate interleaflet coaptation is restored, the results after tightening the PAP suture suggest that, at least in this model, the converse is not true. Relieving apical displacement of the posterior mitral leaflet with PAP as an isolated intervention was not sufficient to abolish CIMR because abnormal septal-lateral interleaflet separation persisted.

Annular or Subvalvular Approach for CIMR?

Rather than favoring either an annular or a subvalvular approach, these observations indicate that successful treatment of CIMR should address both the annular and the papillary muscle geometric distortions whether one applies 2 maneuvers or just 1. It should be remembered that the posterior papillary muscle undergoes complex displacements (lateral, posterior, and toward the annulus) after inferior myocardial infarction. Contrary to current surgical practice, instead of relieving apical leaflet restriction, these results demonstrate that the subvalvular component of successful mitral repair for CIMR should correct lateral displacement of the posterior papillary muscle, as well as restore normal septal-lateral interleaflet coaptation. SLAC induced enough overcorrection of annular dilation in the septal-lateral axis that it pulled the posterior papillary muscle laterally at the subvalvular level. In the absence of such a marked effect by an annular procedure on the subvalvular mitral apparatus, a combined annular-subvalvular approach, such as papillary muscle relocation combined with ring annuloplasty (as described by Kron and coworkers¹²) or the Coapsys device,²⁶ would be necessary and would probably provide superior results compared with ring annuloplasty alone for patients with CIMR. As the results with SLAC show, however, simply undersizing of the annular septal-lateral diameter, if radical enough to also correct subvalvular geometry, is sufficient to reduce CIMR, at least in the short term. These insights into the importance both of septal-lateral annular diameter and lateral displacement of the posterior papillary muscle in the pathogenesis and treatment of CIMR should contribute to more rational design of newer reparative procedures for this vexing disease.

Limitations

This study used a model of ovine inferior LV infarction that differs from the clinical entity in some respects. The sheep have all undergone opening of the pericardium, cardiopulmonary bypass, and surgical manipulation of the mitral apparatus. Also, differences in ventricular and coronary anatomy between sheep and human subjects might influence the remodeling in chronic infarction. Specifically, ovine coronary anatomy is comparatively much more consistent than human anatomy: all sheep have left dominant coronary anatomy; as described by Llaneras and colleagues,¹¹ the second and third obtuse marginal coronary arteries usually supply the ventricle overlying the posterior papillary muscle. We have no data on LV remodeling beyond 7 weeks after myocardial infarction or on the long-term effects of SLAC or PAP on CIMR or mitral geometry. We hope to address these unanswered questions in future experiments.

Quantitative measures of MR, such as estimated regurgitant orifice and regurgitant volume, have shown promise in the research studies of CIMR.^{18,22} In this experiment severity of MR was graded semiquantitatively and subjectively on a scale of 0 to 4+ (a standard method used in clinical practice) by the same echocardiographer (DL). Increased separation between the esophagus and the heart in sheep compared with human subjects resulted in variable echocardiographic image quality, precluding the calculation of more quantitative measures of MR.

Finally, we did not correct lateral displacement of the posterior papillary muscle independent of annular undersizing; thus the importance of normalizing posterior papillary displacement in the lateral axis is inferred from the observation that PAP (which did not reduce MR) normalized annular septal-lateral diameter but not lateral displacement of the posterior papillary muscle. Thus it remains possible that marked annular undersizing in the septal-lateral axis as a solitary intervention is all that is needed.

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Discussion

Dr Thoralf Sundt (Rochester, Minn). Thanks, Fred. This is a beautifully presented work, as we have come to expect from you and from Craig's laboratory. You have also provided me with a beautifully written manuscript. This kind of work exemplifies the true value of a surgical laboratory. These are the kinds of questions that really only surgeons understand and that, in my view, only surgeons can explore in the laboratory. This is real translational research and is a beautiful example of something moving from the clinic to the research laboratory with the aim to apply what is learned back into clinical application. I applaud you for that.

I have a couple of questions that will help to clarify this work for me and perhaps for others. For one, I am intrigued that 3 of the animals in whom you created the infarcts did not have MR. Why not? In terms of the mechanics of the wall motion and the effect on the mitral geometry, what do you think was different about those 3 animals that did not have MR? What can we learn from that group of animals?

Dr Tibayan. Thank you very much, Dr Sundt, for your very kind comments and your always insightful questions.

We actually looked at this discrepancy when we were first developing the model a couple of years ago. It boils down to variations in coronary anatomy that lead to different sizes and locations of the infarcts. When we were first starting out, we ended up with 3 groups of sheep: those with very large infarcts that died acutely, those with smaller infarcts that 2 months later did not leak or leaked very little, and those with kind of medium-sized infarcts in which CIMR developed. Examining and comparing the geometries 7 weeks after infarction, the differences between the leakers and the nonleakers boiled down to increased dilation of the septal lateral annular diameter, more lateral displacement of the posterior papillary muscle, and also more restriction of the posterior leaflet toward the apex. I think those are at least geometrically the differences between those 2 groups.

Dr Sundt. Second, did I understand from the manuscript correctly that in this model the papillary muscle actually moves toward the annulus rather than away? I am accustomed to thinking clinically of the papillary muscle as moving away from the annulus along with a regional wall motion abnormality. This has obvious implications for whether this is actually a valid model for the clinical situation.

Dr Tibayan. Another very good observation. Obviously this is an animal model, and the usual caveats about interspecies differences should apply when you are extrapolating to the clinical arena, but we think that another explanation might be at work. The clinical literature on subvalvular remodeling in CIMR is based on echocardiography, and probably the best example of that work is from the Mayo Clinic, Dr Sarrano's *Circulation* article from a few years ago. And when the echocardiographers talk about apical displacement of the posterior papillary muscles, what they are measuring is the distance from the saddle horn to the tip of the

papillary muscle, which is different from the orthogonal to the annular plane, which is our definition of apical displacement. The important thing to think about that measurement is that distance can increase not only with apical displacement but also even displacement laterally and posteriorly, which is what we see in our model, and therefore we hope that our 3-dimensional analysis is adding some new information to our understanding of the pathogenesis of the disease.

Dr Sundt. A third question that actually relates very much to the debate yesterday afternoon relates to the hemodynamics you report. I believe that the hemodynamics and LV dimensions and so on actually did not improve when you fixed the ischemic MR. This is important in the midst of this debate as to whether we can really affect long-term survival by addressing the MR, a question that I think is still unanswered. I would have expected to see your LV dimensions and the hemodynamics improve when you successfully fixed the MR with the SLAC suture.

Dr Tibayan. There was a trend toward slightly increased dP/dt and end-systolic pressure, as well as a small trend toward decreased LV volumes. However, as you rightly point out, these trends did not meet statistical significance. One would hope that, over time, reducing the regurgitant volume would take off some hemodynamic load from the ventricle and might down the road benefit in terms of function and salutary remodeling, but because we did not follow the animals over time, we have no data to address this obviously very important question.

Dr Sundt. I have a final question if I still fall within Robbins' rules of order. If I take the SLAC suture to be the experimental equivalent of the annuloplasty, then your SLAC suture fixed the ischemic MR. You did not need the PAP, and therefore I am confused by the conclusion that you still need to address the papillary muscle. Perhaps you could clarify what the differences are between the SLAC suture and an annuloplasty.

Dr Tibayan. Thank you. The SLAC suture is conceptually similar to an annuloplasty in that it is an annular intervention and the primary goal is to decrease the septal lateral annular diameter, but we think that there is more going on with the SLAC suture than with the conventional undersized annuloplasty ring. Specifically, there is a greater degree of reduction in the septal lateral diameter, such that the posterior papillary muscle is actually dragged in closer to the septum, and this aspect of subvalvular remodeling is exactly what is probably lacking after placement of an annuloplasty ring and might underlie some of these poor results that we are all so unfortunately familiar with in CIMR. Therefore I think the biggest difference is the subvalvular remodeling because of the greater reduction in the septal lateral diameter.

Dr Daniel Wong (Boston, Mass). I really enjoyed your presentation, Dr Tibayan. I have a question for you. Maybe I missed this. You mentioned that there was a significant amount of posterior displacement of the papillary muscle, and I am curious as to whether that might have been responsible for part of the failure of the PAP technique to try to abolish some of that MR.

Dr Tibayan. You are correct that there is a large displacement of the posterior papillary muscle posteriorly: I think it was 9 mm in this particular study. It is certainly possible that if you correct that, it might have had a different effect. Looking at the results that we have, I think that it might not have been the most important aspect of subvalvular distortion simply because the SLAC suture was able to correct the MR without having any effect on the posterior displacement of the papillary muscle, and therefore I think the biggest difference in terms of the changing of the mitral geometries between the SLAC and PAP was, first of all, more reduction of septal lateral diameter and the correction of the lateral displacement of the posterior papillary muscle, suggesting that the correction of the posterior displacement of the papillary muscle might not be as important.

Figure E1. Schematic of marker array showing radiopaque markers and coordinate reference system. Note that for the purposes of illustration, the anterior papillary muscle and posterior papillary muscle are oriented perpendicular to the commissure-commissure axis rather than parallel to the commissure-commissure axis. *P*, Positive posterior axis; *L*, positive lateral axis; *A*, positive apical axis; *APM*, anterior papillary muscle; *PPM*, posterior papillary muscle.