

Mitral Suture Annuloplasty Corrects both Annular and Subvalvular Geometry in Acute Ischemic Mitral Regurgitation

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Background and aim of the study: Papillary muscle displacement is an important element in the pathogenesis of ischemic mitral regurgitation (IMR). The effects of standard ring annuloplasty on subvalvular geometry are incompletely understood. The hypothesis was tested that annular reduction with a Paneth-type suture annuloplasty would correct both annular and papillary muscle geometric abnormalities during acute left ventricular (LV) ischemia.

Methods: Eight adult sheep underwent insertion of an adjustable, double-suture Paneth-type mitral annuloplasty and radiopaque markers on the left ventricle, mitral annulus, leaflet edges, and anterior (APM) and posterior (PPM) papillary muscle tips. Immediately after surgery, 3-D marker coordinates were determined during Control conditions and during proximal left circumflex occlusion before and after tightening the annuloplasty suture.

Results: Acute IMR (MR grade 0.3 ± 0.3 to 2.1 ± 0.4 , Control versus Ischemia) was associated with end-systolic LV dilatation ($+27 \pm 16$ ml, change relative to Control), greater septal-lateral ($+4.6 \pm 3.1$ cm) and commissure-commissure ($+3.3 \pm 1.6$ cm) mitral annu-

lar diameters, longer anterior ($+1.5 \pm 0.9$ cm) and posterior ($+0.6 \pm 0.9$ cm) papillary muscle tethering distances, greater distance from the APM to the anterior commissure ($+0.9 \pm 0.8$ cm), and shorter distance from the PPM to the posterior commissure (-1.3 ± 1.5 cm). Suture annuloplasty corrected the annular and subvalvular changes, and IMR returned to Control levels (0.5 ± 0.5); only LV end-systolic volume (ESV) was different from Control ($+25 \pm 18$ ml) (mean \pm SD, $p < 0.05$ versus Control by RMANOVA and Dunnett's test).

Conclusion: Suture annuloplasty corrected ischemia-induced end-systolic distortions of the entire valvular-ventricular complex (i.e. inter-leaflet separation, mitral annular dilatation in both axes, and papillary muscle displacements), and abolished acute IMR, independent of any change in ESV. A better understanding of the effects of annular reduction on papillary muscle geometry may lead to improved subvalvular mitral repair techniques.

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Current paradigms concerning the pathogenesis and treatment of ischemic mitral regurgitation (IMR) functionally separate the annulus and papillary muscles. For instance, according to Carpentier's classification system, annular dilatation results in type I (non-restricted, non-prolapsed) leaflet motion, while papillary muscle displacement causes type IIIb motion, or apical leaflet restriction (or tethering or 'tenting') during systole. Most investigations of the mechanism by which ring annuloplasty eliminates mitral regurgitation do not consider the effects of annular remodeling

on subvalvular geometry (1,2). Recent experimental evidence indicates, however, that annular and papillary muscle geometries are tightly linked (3). As the leaflet edges - the final pathway of mitral competence - are linked to the papillary muscles by the chordae tendineae, the impact of any surgical intervention on the subvalvular apparatus is important. Given the interdependence of the elemental components of the valvular-ventricular complex, there is a surprising paucity of data addressing the alterations in papillary muscle position resulting from annular reduction. Using a suture annuloplasty method in an ovine model of acute IMR, the hypothesis was tested that this annular intervention would also alter the geometry of the coupled subvalvular apparatus. Annular reduction sufficient to restore leaflet coaptation was also found to re-establish normal geometric relationships between

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the papillary muscles and mitral annulus during acute IMR.

Materials and methods

Surgical preparation

Eight adult sheep were used, and the operative procedure and technique of marker implantation have been described previously in detail (4). A double loop of 2-0 Prolene was placed around the proximal left circumflex coronary artery for the induction of acute posterolateral left ventricular (LV) ischemia sufficient to produce acute IMR. On cardiopulmonary bypass (CPB), radiopaque markers were implanted on the left ventricle, around the mitral annulus, and on the central edge of each leaflet, as shown in Figure 1. A modified Paneth-Burr annuloplasty suture was inserted using a double-armed 2-0 Prolene suture anchored at the right fibrous trigone, running around the annulus (securing each bite on a pledget), and externalized through the mid-lateral annulus to a tourniquet on the epicardial surface (Fig. 2). A similar suture on the other side of the valve was started at the left fibrous trigone and externalized at the same site on a separate tourniquet. The heart was defibrillated, the animal weaned from CPB, and a micromanometer pressure transducer

(PA4.5-X6; Konigsberg Instruments, Inc., Pasadena, CA, USA) placed in the LV chamber through the apex. The animal was then transferred immediately to the experimental catheterization laboratory where it was studied whilst intubated under open-chest, anesthetized (isoflurane 1.5-2.0%) conditions.

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 (DHEW NIHG publication 85-23, revised 1985). This study was approved by the Stanford Medical Center Laboratory Research Animal Review committee and conducted according to Stanford University policy.

Data acquisition

Images were acquired with the animal in the right lateral decubitus position with a biplane videofluoroscopy system (Philips Medical Systems, Pleasanton, CA, USA). Images (at 60 Hz) from two radiographic views were digitized and merged to yield 3-D coordinates for each of the radiopaque markers using custom-designed software. Ascending aortic pressure, LV pressure, and ECG voltage signals were recorded simultaneously during marker data acquisition.

For each animal, three consecutive steady-state beats during control conditions, circumflex ischemia, and ischemia with annuloplasty suture (ASP, Annuloplasty Suture Pull) tightening were designated as Baseline,

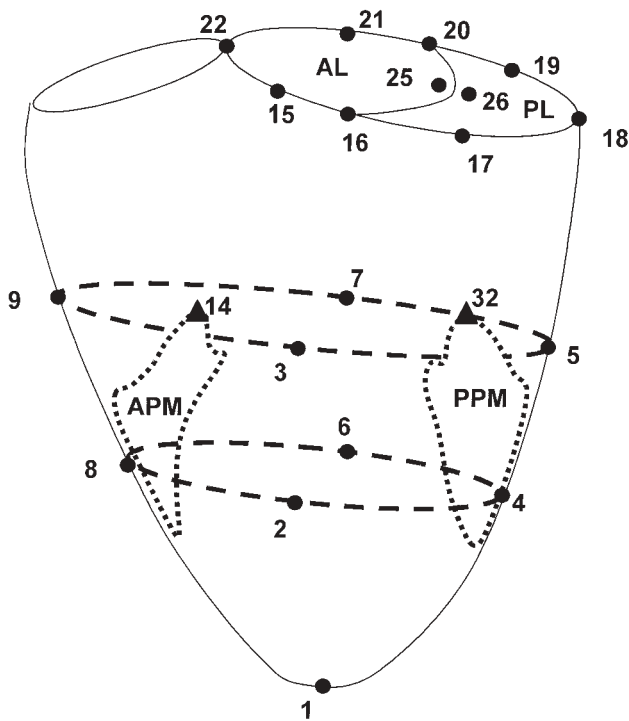


Figure 1: Schematic of radiopaque marker array used in these studies. AL: Anterior mitral leaflet; APM: Anterior papillary muscle; PL: Posterior mitral leaflet; PPM: Posterior papillary muscle.

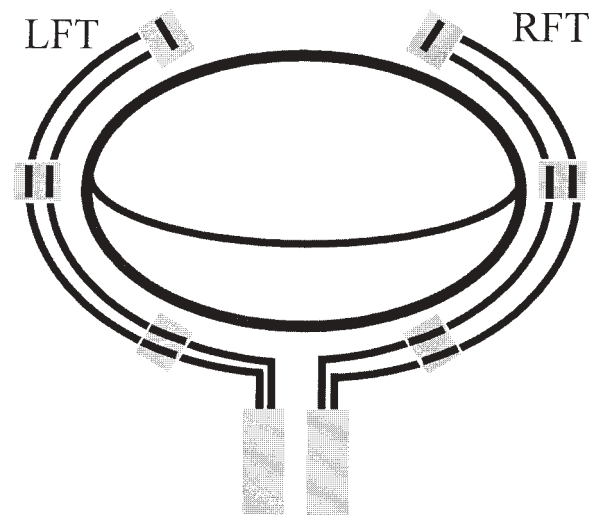


Figure 2: Schematic depiction of the double-suture annuloplasty method employed. A double-armed 2-0 Prolene suture was passed from each fibrous trigone and externalized to an adjustable tourniquet. LFT: Left fibrous trigone; RFT: Right fibrous trigone.

Table I: Hemodynamics.

Parameter	Control	Ischemia	Ischemia + ASP
MR (grade 0-4+)	0.3 ± 0.3	2.1 ± 0.4*	0.5 ± 0.5
HR (bpm)	112 ± 13	100 ± 32	103 ± 20
dP/dt (mmHg/s)	2,656 ± 378	1,876 ± 416*	1,681 ± 318*
LVPmax	128 ± 37	92 ± 8*	91 ± 7*
LVEDP	16 ± 4	23 ± 5*	22 ± 4*

Values are mean ± SD.

*p <0.05 versus Control.

dP/dt: First derivative of LV pressure versus time; HR: Heart rate; LVEDP: Left ventricular end-diastolic pressure; LVP: Left ventricular pressure; MR: Mitral regurgitation.

Ischemia, and Ischemia + ASP, respectively. For each cardiac cycle, end-systole was defined as the frame containing the peak rate of fall in LV pressure (-dP/dt), and end-diastole as the videofluoroscopic frame prior to the upstroke of the LV pressure curve. Instantaneous LV volume was computed from the epicardial LV markers using a multiple tetrahedral volume method. MR was graded by an experienced cardiologist (D.L.) according to the extent and width of the regurgitant jet and categorized as either none (0), trace (0.5+), mild (+1), moderate (+2), moderate to severe (+3), or severe (+4).

Data analysis

With regard to mitral valve geometry, for each time frame the mitral annular area (MAA) was computed from the 3-D coordinates of the eight markers sutured to the mitral annulus by summing eight triangular areas from the annular markers and the annular centroid. The septal-lateral (S-L) annular diameter was calculated as the distance in 3-D space between mark-

ers placed on the mid-septal (#22) and mid-lateral (#18) annulus. The commissure-commissure annular dimension was calculated as the distance between markers #16 and #20. Papillary muscle position was measured as the 3-D distance from each papillary muscle tip (anterior papillary muscle, #14; posterior papillary muscle, #32) to the mid-septal annulus marker (#22), the distance from the anterior papillary muscle tip to the anterior commissure (#16), and the distance from the posterior papillary muscle tip to the posterior commissure (#20). Inter-leaflet separation was calculated as the distance between leaflet edge markers (#25 and 26) along the S-L valve axis.

Statistical analysis

All data were reported as mean ± SD, unless otherwise stated. Hemodynamic and marker-derived data from consecutive steady-state beats from each heart were time-aligned at end-systole (t = 0). Group mean hemodynamic and end-systolic mitral valve geometric data for Ischemia and Ischemia + ASP were compared

Table II: Mitral valve and subvalvular geometry at end-systole.

Parameter	Control	Ischemia	Ischemia + ASP
LVESV (ml)	100±35	127±42*	125±44*
S-L diameter (mm)	22.8±2.9	27.4±3.6*	21.4±2.9
C-C diameter (mm)	30.5±4.1	33.8±3.7*	29.4±5.1
PPM to saddlehorn (mm)	48.8±8.8	49.4±8.6*	48.8±8.8
APM to saddlehorn (mm)	42.9±3.8	44.4±4.2*	43.6±4.0
PPM to PCOM (mm)	39.7.0±7.0	38.4±7.7*	39.6±7.5
APM to ACOM (mm)	34.2±3.1	35.1±3.1*	34.3±3.2
Leaflet separation (mm)	1.6±0.2	1.9±0.3*	1.7±0.3

Values are mean ± SD.

*p <0.05 versus Control.

APM to ACOM: Distance from anterior papillary muscle tip to anterior commissure at end-systole; APM to saddlehorn: Distance from anterior papillary muscle tip to mitral annular saddlehorn at end-systole; C-C diameter: Commissure-commissure diameter; Leaflet separation: Distance between anterior and posterior leaflet edge markers at end-systole; LVESV: Left ventricular end-systolic volume; PPM to PCOM: Distance from posterior papillary muscle tip to posterior commissure at end-systole; PPM to saddlehorn: Distance from posterior papillary muscle tip to mitral annular saddlehorn at end-systole; S-L diameter: Septal-lateral annular diameter.

to Baseline using repeated measures analysis of variance (RMANOVA) with Dunnett's test.

Results

The group mean hemodynamic data at baseline, during acute circumflex ischemia, and during ischemia plus ASP cinching are summarized in Table I. During ischemia, the heart rate did not change, MR and LV end-diastolic pressure (LVEDP) increased significantly, and dP/dt and maximum LV pressure were each decreased. Tightening of the suture annuloplasty eliminated the MR, but did not affect heart rate, dP/dt, maximum LV pressure, or LVEDP.

The group mean valvular-ventricular complex geometric data at end-systole are summarized in Table II. Acute ischemia resulted in global LV dilatation (increased ESV), larger S-L and commissure-commissure mitral annular dimensions, and displacement of both papillary muscles away from the annular saddlehorn. The posterior papillary muscle tip moved closer to the posterior commissure, and the anterior papillary muscle tip moved away from the anterior commissure. These changes were associated with increased inter-leaflet separation and mitral regurgitation.

Suture annuloplasty cinching did not affect global LV size, but returned the annular dimensions and papillary muscle distances to baseline levels. Coincident with the restoration of annular and papillary muscle geometry, leaflet separation decreased to baseline, and MR was abolished. Figure 3 shows the significant changes from Control in global, annular, subvalvular, and leaflet 3-D geometry during Ischemia and Ischemia + ASP. Annular reduction normalized local annular and subvalvular geometry without reducing ESV.

Discussion

Ischemic mitral regurgitation remains a challenging clinical problem for cardiac surgeons. The postoperative outcome for patients with IMR is markedly inferior to that of individuals with other causes of MR, and residual and/or recurrent IMR occurs in upwards of 30% or more of patients at medium-term follow up (5), which worsens the already poor prognosis independent of the degree of underlying LV systolic dysfunction (6). These suboptimal surgical results might be improved if a better understanding was available of how mitral annular size reduction - the preferred cur-

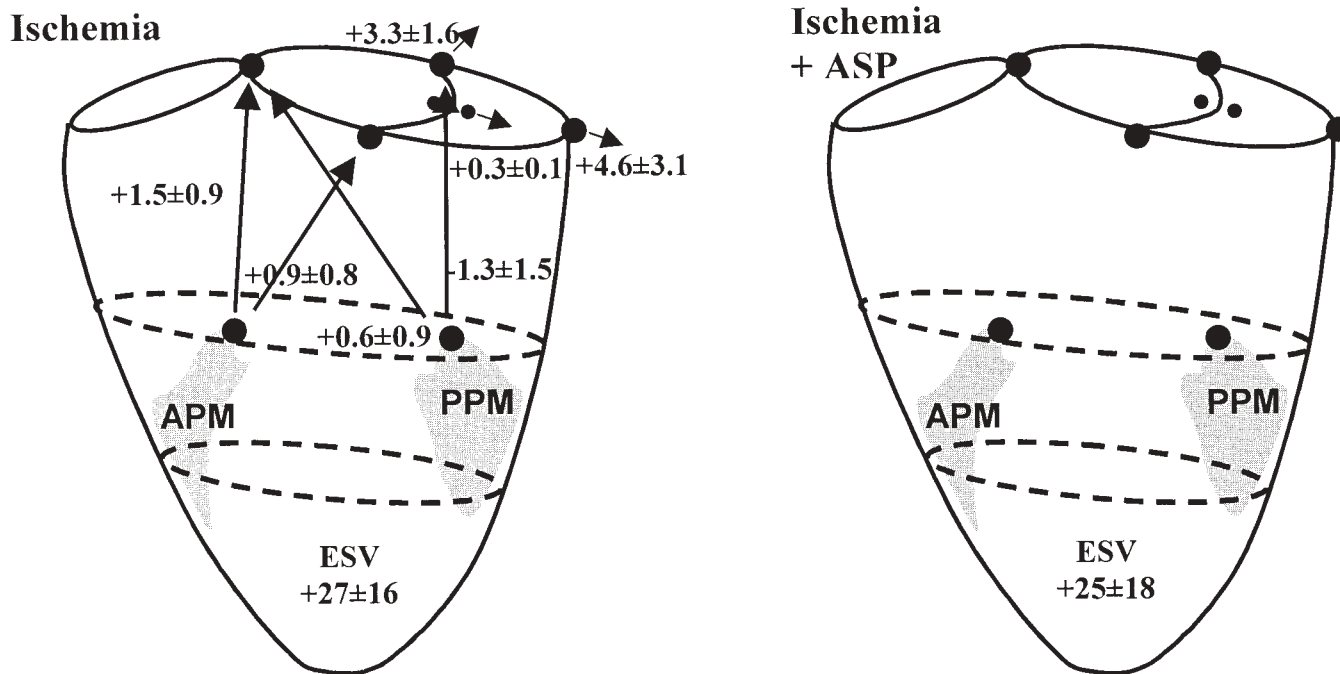


Figure 3: Graphical summary of the end-systolic changes in annular, leaflet, subvalvular, and left ventricular (LV) 3-D geometry. Arrows represent statistically significant changes (mean \pm SD) between Control and Ischemia (left) and Ischemia + annuloplasty suture tightening (ASP) (right) at end-systole. During Ischemia (left), all geometric measurements changed compared to Control: Septal-lateral and commissure-commissure annular diameters, leaflet separation, posterior papillary muscle to annular saddlehorn distance, posterior papillary muscle to posterior commissure, anterior papillary muscle to saddlehorn, anterior papillary muscle to anterior commissure, and LV end-systolic volume (ESV). Annular reduction with ASP (right) normalized end-systolic annular, subvalvular, and leaflet geometric abnormalities, but ESV was still larger than Baseline. APM: Anterior papillary muscle; PPM: Posterior papillary muscle.

rent treatment method for IMR - impacts upon the geometry of the subvalvular apparatus, which commonly is perturbed (7,8). The conventional view of the mechanism of ring annuloplasty in patients with IMR is that annular reduction eliminates annular dilatation, thereby enhancing leaflet coaptation (2), but the effects of annular remodeling on subvalvular geometry are generally not considered (9). This situation is acceptable if the main problem is IMR due to type I leaflet motion secondary to annular dilatation, but is clearly a problem if type IIIb leaflet motion (systolic apical restriction, tethering, or 'tenting') is also present.

The results of this acute IMR experiment support an earlier view proposed by Dagum et al. that the geometries of the annulus and papillary muscles are tightly linked, and the corollary that any annular remodeling procedure will alter subvalvular geometry (3). In this case, annular reduction with an adjustable suture annuloplasty during acute ischemia normalized the end-systolic geometric relationships of the papillary muscles with respect to the annulus and abolished MR without affecting end-systolic LV size.

The geometric and functional coupling of the mitral annulus and the papillary muscles has been supported by other animal investigations. Komeda et al. observed that in normal dogs a 'J-shaped complex' consisting of the papillary muscle and LV wall maintained the papillary muscle tips at a constant distance below the annulus through a variety of hemodynamic alterations during the entire cardiac cycle (10). Dagum et al. also reported that papillary muscle to mitral annulus distances were constant throughout the cardiac cycle in normal sheep, but that these relationships were disrupted during acute LV ischemia, leading to leaflet malcoaptation and IMR (3). Thus, because of the geometric interdependence of the entire valvular-ventricular complex, neither the annulus nor the papillary muscles can be perturbed in isolation. It follows from that proposition that any intervention which remodels the annulus will have a direct effect on papillary muscle position, geometry and motion.

In the present study of acute IMR, LV ischemia caused annular dilatation and altered the end-systolic positions of the papillary muscles with respect to the annulus. Both papillary muscle tips moved away from the annular saddlehorn, the posterior papillary muscle tip moved closer to the posterior commissure, while the anterior papillary muscle tip moved away from the anterior commissure. These end-systolic geometric perturbations were associated with mitral leaflet separation and IMR. Tightening the annuloplasty suture not only corrected the annular dilatation, as expected, but also normalized the displacement of the papillary muscles and inter-leaflet separation and reduced the degree of IMR. Interestingly, these papillary tip to

annulus distances were normalized independent of any change in global end-systolic LV size - that is, local remodeling of the subvalvular apparatus was associated with normalization of the annular, as opposed to global, LV end-systolic geometry. By the same token, interventions aimed at remodeling the subvalvular apparatus may have effects on annular geometry mediated by the same coupling mechanisms. Kron and associates have recently described surgical relocation of the papillary muscle by means of a suture between the posterior papillary muscle tip and the mitral annulus (11). In the experimental setting, infarct plication and papillary muscle repositioning with an external device are effective in altering papillary muscle geometry in sheep with chronic IMR (12,13). It is possible that some of the effects of these 'subvalvular' procedures may be due to salutary remodeling of the mitral annulus.

The importance of the mitral subvalvular apparatus in the genesis of functional MR has been underscored by clinical and experimental studies demonstrating that papillary muscle displacement causes systolic tenting of the leaflets (type IIIb motion) and leaflet malcoaptation (1,8). In an ovine model of chronic IMR, Otsuji et al. found that the distance from the papillary tips to the saddlehorn was the only independent predictor of regurgitant volume (7). Lai et al., from the present authors' laboratory, demonstrated in an acute IMR preparation that papillary muscle tip displacement away from the lateral annulus predicted posterior leaflet systolic restriction and IMR (14). Because the chordae tendineae maintain the papillary tip to leaflet edge distances constant (3,4), leaflet coaptation is exquisitely sensitive to changes in subvalvular geometry. Therefore, even small papillary muscle displacements - as were observed in the present study and others - may have a critical impact on valve competence (4,15).

The results of the present study support the hypothesis that the papillary muscles must maintain proper positioning with respect to the mitral annulus in order for the valve to be competent. Acute ischemia altered the relationship of each papillary muscle to the saddlehorn and its respective commissure. Tightening the suture annuloplasty reversed the perturbations induced by acute ischemia and restored the baseline annular-subvalvular relationships, moving the posterior papillary muscle tip further from the posterior commissure, the anterior papillary muscle tip closer to the anterior commissure, and both papillary muscles closer to the saddlehorn.

Annular reduction, especially in the S-L dimension (16), is probably the predominant means by which annuloplasty restores leaflet coaptation. These data demonstrate however that previously unrecognized

subvalvular remodeling also occurs, probably plays a role after successful ring annuloplasty, and deserves further investigation. This shift to a more global view of the mitral valvular-ventricular complex may lead to better reparative techniques. For example, residual IMR after annuloplasty may be due in part to failure to restore adequately the pathological derangements in papillary muscle geometry. An enhanced understanding of annular and subvalvular relationships might lead to ways in which annular size and shape may be changed, and the papillary muscle tip position optimized. For example, an annuloplasty ring may be designed that minimizes only S-L annular diameter (versus commissure-commissure) and papillary muscle to annular saddlehorn distance. The choice of annuloplasty ring size may also be influenced by the concomitant subvalvular effects of remodeling the annulus. Specifically, an undersized ring, which currently is advocated for patients with chronic ischemic MR in order to decrease LV wall stress (17), may have the unexpected benefit of correcting papillary muscle displacement. New mitral valve repair techniques, such as the Alfieri stitch (9) or septal-lateral annular cinching ('SLAC') (16) could be evaluated or refined on the basis of their potential to address subvalvular geometric perturbations in the setting of functional MR. In cases where annuloplasty alone is unable to correct the distorted subvalvular apparatus or extensive type IIIb leaflet motion is present, adjunctive procedures such as papillary muscle re-attachment or relocation (11) should be considered.

Study limitations

The results of this experiment of acute IMR in open-chest, anesthetized, normal sheep cannot apply directly to the clinical scenario of chronic IMR where the annular and subvalvular components have remodeled over time. Recent studies of chronic IMR suggest, however, that the geometric perturbations in acute IMR are at least qualitatively similar to those seen in experimental preparations of chronic IMR with respect to annular dilatation and papillary muscle displacement (8). Whilst ring annuloplasty is the current clinical treatment of choice for patients with IMR, the present experiment used a reversible suture annuloplasty in order to compare baseline, ischemia and annuloplasty data in the same group of animals. Finally, these studies were focused solely on changes at end-systole.

Quantitative measures of MR, such as estimated regurgitant orifice and regurgitant volume, are promising based on studies of chronic ischemic MR in humans (7,18). In the present study, the severity of MR was graded only semi-quantitatively and subjectively by jet size. Increased separation between the esopha-

gus and heart in sheep relative to humans resulted in highly variable echocardiographic image quality, thereby precluding the calculation of more quantitative measures of MR.

The elimination of acute ischemic MR with the ASP suture did not improve hemodynamics (e.g., higher dP/dt , lower LVEDP) as might be expected. This was most likely due to the additional myocardial ischemia due to proximal circumflex occlusion endured by the animals when the ASP suture was tightened, which probably overwhelmed any salutary effects of reducing MR.

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