The effect of pure mitral regurgitation on mitral annular geometry and three-dimensional saddle shape

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Objective: Chronic ischemic mitral regurgitation is associated with mitral annular dilatation in the septal-lateral dimension and flattening of the annular 3-dimensional saddle shape. To examine whether these perturbations are caused by the ischemic insult, mitral regurgitation, or both, we investigated the effects of pure mitral regurgitation (low pressure volume overload) on annular geometry and shape.

Methods: Eight radiopaque markers were sutured evenly around the mitral annulus in sheep randomized to control (CTRL, n = 8) or experimental (HOLE, n = 12) groups. In HOLE, a 3.5- to 4.8-mm hole was punched in the posterior leaflet to generate pure mitral regurgitation. Four-dimensional marker coordinates were obtained radiographically 1 and 12 weeks postoperatively. Mitral annular area, annular septal-lateral and commissure–commissure dimensions, and annular height were calculated every 16.7 ms.

Results: Mitral regurgitation grade was 0.4 ± 0.4 in CTRL and 3.0 ± 0.8 in HOLE ($P < .001$) at 12 weeks. End-diastolic left ventricular volume index was greater in HOLE at both 1 and 12 weeks; end-systolic volume index was larger in HOLE at 12 weeks. Mitral annular area increased in HOLE predominantly in the commissure–commissure dimension, with no difference in annular height between HOLE versus CTRL at 1 or 12 weeks, respectively.

Conclusion: In contrast with annular septal-lateral dilatation and flattening of the annular saddle shape observed with chronic ischemic mitral regurgitation, pure mitral regurgitation was associated with commissure–commissure dimension annular dilatation and no change in annular shape. Thus, infarction is a more important determinant of septal-lateral dilatation and annular shape than mitral regurgitation, which reinforces the need for disease-specific designs of annuloplasty rings.

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This work was supported by Grants HL-29589 and HL-67025 from the National Heart, Lung and Blood Institute. Doctors Nguyen was a Leah McConnell Cardiovascular Surgical Research Fellow and recipient of the Thoracic Society Foundation Research Fellowship Award. Dr Itoh received funding from the Uehara Memorial Foundation, and Dr Carlhäll received funding from the Swedish Heart and Lung Foundation and the County Council of Östergötland, Sweden. Dr Bothe received stipend support from the Deutsche Herzstiftung.

Presented at the 87th Annual Meeting of the American Association for Thoracic Surgery Washington, DC, May 2007.

Received for publication May 23, 2007; revisions received Nov 26, 2007; accepted for publication Dec 18, 2007.

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J Thorac Cardiovasc Surg 2008;136:557-65

0022-5223/$34.00

doi:10.1016/j.jtcvs.2007.12.087

Chronic ischemic mitral regurgitation (IMR) is a common sequela of ischemic heart disease, with a prevalence estimated at 1.6 to 2.8 million patients in the United States.[1] The clinical consequence of severe, uncorrected mitral regurgitation (MR) is excess morbidity and mortality.[2] In recent years, much has been learned about the pathophysiology of chronic IMR. We now know that chronic IMR results in mitral annular dilatation, predominantly in the septal-lateral (SL) dimension,[3] and alterations in annular 3-dimensional (3D) saddle shape[4,5] in sheep and humans, which has guided the evolution of annuloplasty rings and novel medical devices. Whether these perturbations are catalyzed by the ischemic insult to the left ventricle, the volume overload from MR, or both, is unknown. In an effort to dissect

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Abbreviations and Acronyms

ED = end diastole
ES = end systole
CC = commissure–commissure
IMR = ischemic mitral regurgitation
LV = left ventricular
MR = mitral regurgitation
SL = septal-lateral
3D = 3-dimensional
TTE = transthoracic echocardiography

the role of low pressure volume overload on mitral annular geometry, dynamics, and shape, we developed a chronic ovine model of pure MR and tested the hypotheses that pure MR symmetrically increases mitral annular area and flattens annular 3D saddle shape.

Materials and Methods

All animals received humane care in compliance with guidelines sets forth by the National Institutes of Health (US Department of Health and Human Services National Institutes of Health 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.

Surgical Preparation

Sheep were premedicated with ketamine (25 mg/kg, intramuscularly) and randomized to either control (CTRL, n = 8) or experimental (HOLE, n = 12) groups. Anesthesia was induced with sodium thiopental (6.8 mg/kg, intravenously) and maintained with inhalational isoflurane (1%–2.5%). Epicardial echocardiography was used to qualitatively grade (0–4) MR at baseline on the basis of color Doppler regurgitant jet extent and width.[6,7] Through a left thoracotomy, 12 tantalum myocardial markers were inserted in the left ventricular (LV) subepicardium and septum along 4 equally spaced longitudinal meridians, with 1 marker at the LV apex. After establishment of cardiopulmonary bypass, 8 tantalum markers were sutured evenly around the circumference of the mitral annulus via an atriotomy, 1 near each commissure (numbers 1 and 5) and 3 along the septal (numbers 2, 3, and 4) and lateral (numbers 6, 7, and 8) annular perimeter (Figure 1, *A*). In HOLE, a 3.5- to 4.8-mm hole was created in the middle scallop of the posterior mitral leaflet using an aortic hole puncher to generate MR (Figure 1, *B* and *C*). The atriotomy was closed, the heart was deaired, the crossclamp was removed, and the heart was defibrillated (mean cardiopulmonary bypass time 65 ± 5 minutes; mean aortic crossclamp time 30 ± 4 minutes). An implantable micromanometer pressure transducer (PA4.5-X6; Konigsberg Instrument, Inc, Pasadena, Calif) was placed in the LV chamber through the apex and exteriorized through the skin between the scapulae. The chest was closed, and the animal recovered.

Study Group

Fifty-eight sheep were initially randomized to either the CTRL (n = 25) or HOLE (n = 33) group. Intraoperatively, 9 sheep had natural moderate-severe MR and were excluded. We were unable to wean 4 sheep from cardiopulmonary bypass, and 1 sheep expired from technical/accidental complications. A total of 9 perioperative complications occurred (stroke [n = 3] and pulmonary edema [n = 6]). Four animals were excluded because of insufficient MR despite creating a hole in the posterior mitral leaflet (a smaller 2.8-mm hole was used in 3 of the 4 animals). Three animals expired from unknown causes (necropsy results were unrevealing). Eight sheep were excluded because of either missing or poorly placed markers, leaving a remaining total of 20 animals (CTRL, n = 8; HOLE, n = 12) for analysis.

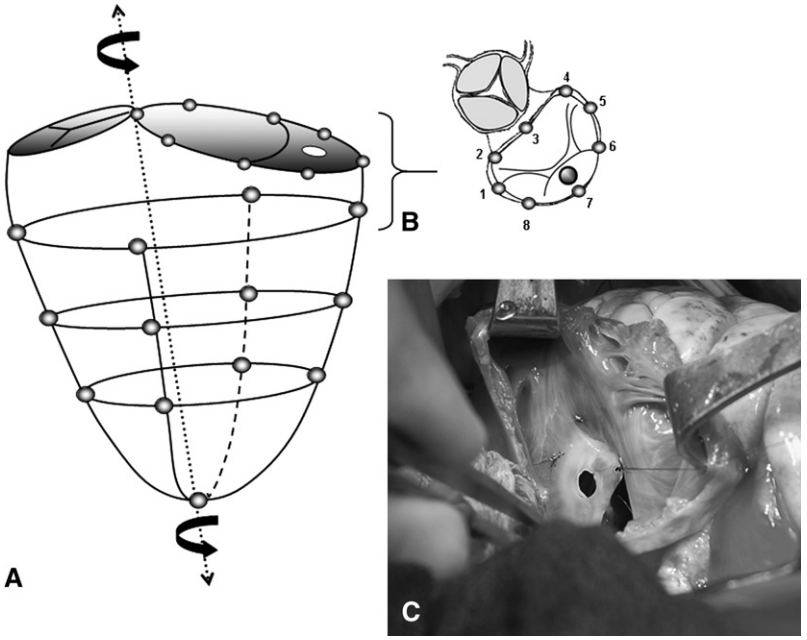

Figure 1. A, Locations of LV epicardial markers (shaded circles) surgically implanted to silhouette the LV chamber along 4 equally spaced longitudinal meridians. B, Schematic representation of the 8 marker array on the mitral annulus, as viewed from the left atrium. Marker numbers (1–8) are shown. The location of the hole in the middle scallop of the posterior mitral leaflet is shown as a shaded circle. C, Intraoperative photograph as viewed from the left atrium of mitral annular markers with a 4.8-mm hole in the middle scallop of the posterior mitral leaflet.

Experimental Protocol

After an acclimatization period of 7 ± 1 days, animals were taken to the cardiac catheterization laboratory, sedated with ketamine, intubated, mechanically ventilated, and maintained with inhalational isoflurane. A micromanometer catheter (Millar Instruments, Inc, Houston, Tex) was introduced through a sheath in the left carotid artery and advanced to the aortic arch for aortic pressure measurement. Transthoracic echocardiography (TTE) and simultaneous biplane videofluoroscopic marker data and hemodynamic data were acquired. MR was then graded by a blinded expert echocardiographer (D.L.) on the basis of color Doppler regurgitant jet extent and width.[6] The animal was then stabilized and recovered. All animals were followed for clinical signs of heart failure (tachypnea, lethargy, and anorexia). TTE was performed by our blinded echocardiographer weekly to grade MR and detect LV dilatation. After 12 ± 1 weeks, the animals returned to the cardiac catheterization laboratory for recording of hemodynamic, TTE, and marker data.

Data Acquisition and Analysis

Images were acquired with animals in the right lateral position with a biplane videofluoroscopy system (Philips Medical Systems, North America Company, Pleasanton, Calif). Data from the 2 radiographic views were digitized and merged to yield 3D coordinates for each marker every 16.7 ms using custom software.[8] The accuracy of 3D reconstructions from biplane videograms of length measurements, expressed as mean percentage error of a known marker-to-marker 3D length has been shown to be 0.2% with a reproducibility of 1%.[9] Aortic pressure, LV pressure, and electrocardiogram voltage signals were digitized and recorded simultaneously during marker data acquisition.

Three consecutive steady-state beats in sinus rhythm were selected for analysis from each study. For each cardiac cycle, end diastole (ED) was defined as the maximal second derivative of LV pressure, corresponding to the upstroke of LV pressure. End systole (ES) was defined as the videofluoroscopic frame before the time of peak negative LV rate of pressure decrease ($-dP/dt_{max}$). Instantaneous LV volume was calculated from LV markers by multiple tetrahedra constructed from the marker coordinates and corrected for LV convexity.[10] Although myocardial volume is included in the calculation of LV volume, relative changes in LV chamber size are accurately measured.

Mitral Annular Geometry

Mitral annular area in 3D space was calculated for each frame throughout the cardiac cycle as the sum of the areas of 8 triangles formed by consecutive adjacent marker pairs on the annulus and the annular centroid defined by markers 1 to 8 (Figure 1, *B*). The SL diameter of the annulus was calculated as the distance in 3D space between the 2 markers placed in the middle of the septal and lateral mitral annulus, respectively (3 and 7, Figure 1, *B*). The commissure–commissure (CC) diameter was calculated as the distance in 3D space between the 2 annular commissural markers (1 and 5, Figure 1, *B*). Mitral annular height was calculated as the orthogonal distance from the saddlehorn marker (3, Figure 1, *B*) to the least-squares mitral annular plane defined without considering the saddlehorn marker.

Statistical Analysis

Data are reported as mean ±1 standard deviation unless otherwise specified. Hemodynamic and marker-derived data from consecutive steady-state beats from each heart were time aligned at either ED or ES. Marker data were calculated over 20 frames before and after either ED or ES, thus allowing evaluation over a time period of 700 ms. Data were compared using 2-way repeated-measures analysis of variance with the Bonferroni post hoc test for multiple comparisons (Sigmastat 3.5, Systat Software Inc, San Jose, Calif).

Results

Hemodynamic data for CTRL and HOLE are shown in Table 1. There was no difference in heart rate, weight, and body surface area between CTRL and HOLE at 1 and 12 weeks. MR was significantly greater in HOLE versus CTRL at 1 and 12 weeks (1 week: 3.2 ± 0.9 vs 0.5 ± 0.6; 12 weeks: 3.0 ± 0.8 vs 0.4 ± 0.4, all $P < .001$), Table 1. At 12 weeks, LV mass index, however, was greater in HOLE than CTRL (198.5 ± 11.2 g/m^2 vs 170.2 ± 13.2 g/m^2, $P = .002$). LV ED volume index was larger in HOLE versus CTRL at both 1 and 12

TABLE 1. Hemodynamics

	1 wk		12 wk	
	CTRL	HOLE	CTRL	HOLE
MR	0.5 ± 0.6	3.2 ± 0.9[a]	0.4 ± 0.4	3.0 ± 0.8[a]
HR (min^{-1})	107 ± 17	100 ± 10	103 ± 11	98 ± 10
Weight (kg)	55.2 ± 4.7	54.3 ± 12.9	58.5 ± 7.1	56.2 ± 4.4
BSA (m^2)	1.15 ± 0.06	1.13 ± 0.17	1.19 ± 0.09	1.17 ± 0.06
LV mass index (g/m^2)			170.2 ± 13.2	198.5 ± 11.2[a]
EDVI (mL/m^2)	104.1 ± 19.0	131.6 ± 15.1[a]	109.1 ± 30.0	146.3 ± 30.3[a]
ESVI (mL/m^2)	80.3 ± 16.7	97.0 ± 14.7	81.7 ± 29.5	106.3 ± 18.7[a]
EDP (mm Hg)	16.0 ± 5.3	19.0 ± 2.7	14.9 ± 2.8	16.9 ± 1.3

MR, Mitral regurgitation; *HR,* heart rate (min^{-1}); *BSA,* body surface area (m^2); *LV mass index,* left ventricular mass indexed by BSA (g/m^2); *EDVI,* end-diastolic volume indexed by BSA (mL/m^2); *ESVI,* end-systolic volume indexed by BSA (mL/m^2); *EDP,* end-diastolic pressure (mm Hg). Group mean (±standard deviation).
[a]$P \leq .04$ versus CTRL. Two-way repeated-measures analysis of variance with Bonferroni post hoc for multiple comparisons.

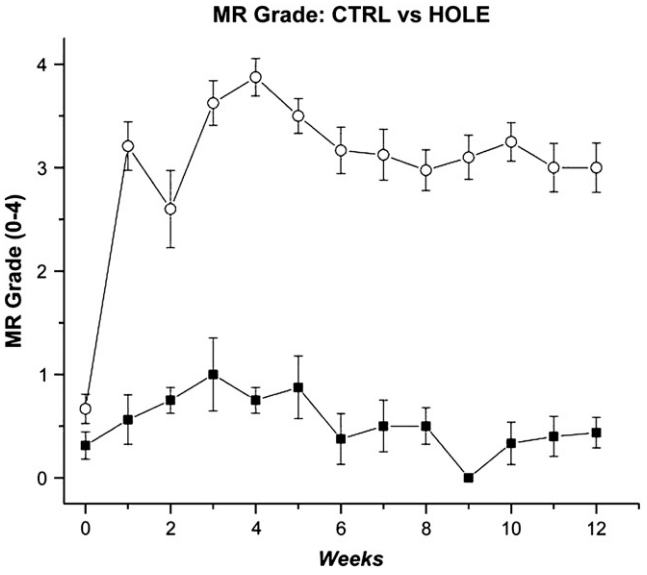

Figure 2. Comparison of MR grade between CTRL (■, closed black squares) and HOLE (○, open circles) as a function of time, weeks (mean ± 1 standard error of the mean). *MR,* Mitral regurgitation.

weeks (1 week: 131.6 ± 15.1 vs 104.1 ± 19.0, $P = .04$, 2 *df*, $F = 2.4$; 12 weeks: 146.3 ± 30.3 vs 109.1 ± 30.0, $P = .01$, 2 *df*, $F = 5.3$), whereas end-systolic volume index was larger in HOLE versus CTRL only at 12 weeks (106.3 ± 18.7 vs 81.7 ± 29.5, $P = .03$, 2 *df*, $F = 4.9$). Figure 2 shows changes in MR grade between CTRL and HOLE throughout the study time course.

Figure 3 summarizes mitral annular dynamics time-aligned at ED, and Table 2 shows annular geometry at ED and ES at 12 weeks. There was a significant increase in mitral annular area, CC, and SL dimensions at 12 weeks in HOLE versus CTRL, with a predominant increase in CC relative to SL dimension.

To assess changes in mitral annular 3D shape, we calculated annular height throughout the cardiac cycle with data time aligned at ES (Figure 4). At both 1 and 12 weeks, there was no difference in annular height between CTRL and HOLE. To obtain a more complete picture of 3D geometry of the entire annulus, the displacement of each annular marker from the least-squares annular plane was calculated at ED and ES (Figure 5). There was no difference in marker displacement from the least-square annular plane between CTRL and HOLE at ED or ES.

Discussion

To understand the contribution of chronic pure MR to mitral annular remodeling without the confounding effects of LV ischemia or infarction, we developed a chronic ovine model of pure low pressure LV volume overload MR and examined the effects of pure MR on mitral annular geometry and dynamics. In this chronic ovine study, pure MR resulted in mitral annular dilatation predominately in the CC dimension and no change in mitral annular 3D shape.

Chronic Ovine Model of Mitral Regurgitation

MR imposes a pure low-pressure volume overload on the LV, whereas excess volume is ejected into the low-impedance left atrium during systole with either normal or subnormal LV systolic pressure.[11] Increased ED stress causes replication of sarcomeres in series and compensatory eccentric LV hypertrophy.[12] Although MR is a common phenomenon, most previous studies of LV volume overload have used high-pressure experimental models in which excess LV volume is ejected into the high pressure aortic system against a competent mitral valve.[13-19] Other experimental models relied on division of chordae tendineae,[20,21] which can result in deterioration of global LV systolic function.[22,23] Our chronic closed-chest ovine model of "low-pressure" volume overload does not appear to *directly* affect LV systolic function. By placing a predefined hole in the posterior mitral leaflet (Figures 1, *C* and 2), we were able to reproducibly create low-pressure volume overload.

Annular Geometry and Dynamics

Chronic ovine IMR remodels the mitral annulus by increasing mitral annular area predominantly in the SL dimension.[3,24] Because of the inherent dual nature of the insult, however, it is unclear whether these changes occur from LV infarction, volume overload from MR, or both. In this study, chronic pure MR without infarction increased mitral annular area primarily in the mitral CC dimension (Figure 3). These findings suggest that infarction may be a more important determinant of increased SL annular dilatation than LV volume overload, which has spawned a new generation of disease-specific IMR/FMR (Functional mitral regurgitation) annuloplasty rings (Edwards GeoForm and IMR ETlogix rings; Edwards Lifesciences, Irvine, CA; St Jude Medical RSR ring, St Jude Medical Inc, St Paul, Minn).

It is widely held that MR begets MR in a self-perpetuating cycle,[1] although this supposition has not been directly tested experimentally. Myocardial infarction distorts the LV, resulting in papillary muscle displacement, impaired leaflet coaptation, and MR.[1] LV dilatation leads to annular enlargement, thereby exacerbating valvular incompetence in a vicious cycle. It is interesting to note that in this study, however, MR did not beget MR. Specifically, despite an observed increase in mitral annular area and ventricular dilatation, there were minimal changes in MR grade throughout the study (Figure 2, Table 1). Several possible explanations exist for this observation: (1) The time course of the study may not have been sufficient to increase mitral annular area to a large enough degree where the annular dilatation would enhance the progression of MR; (2) the amount of MR vis-à-vis regurgitant fraction and the effective

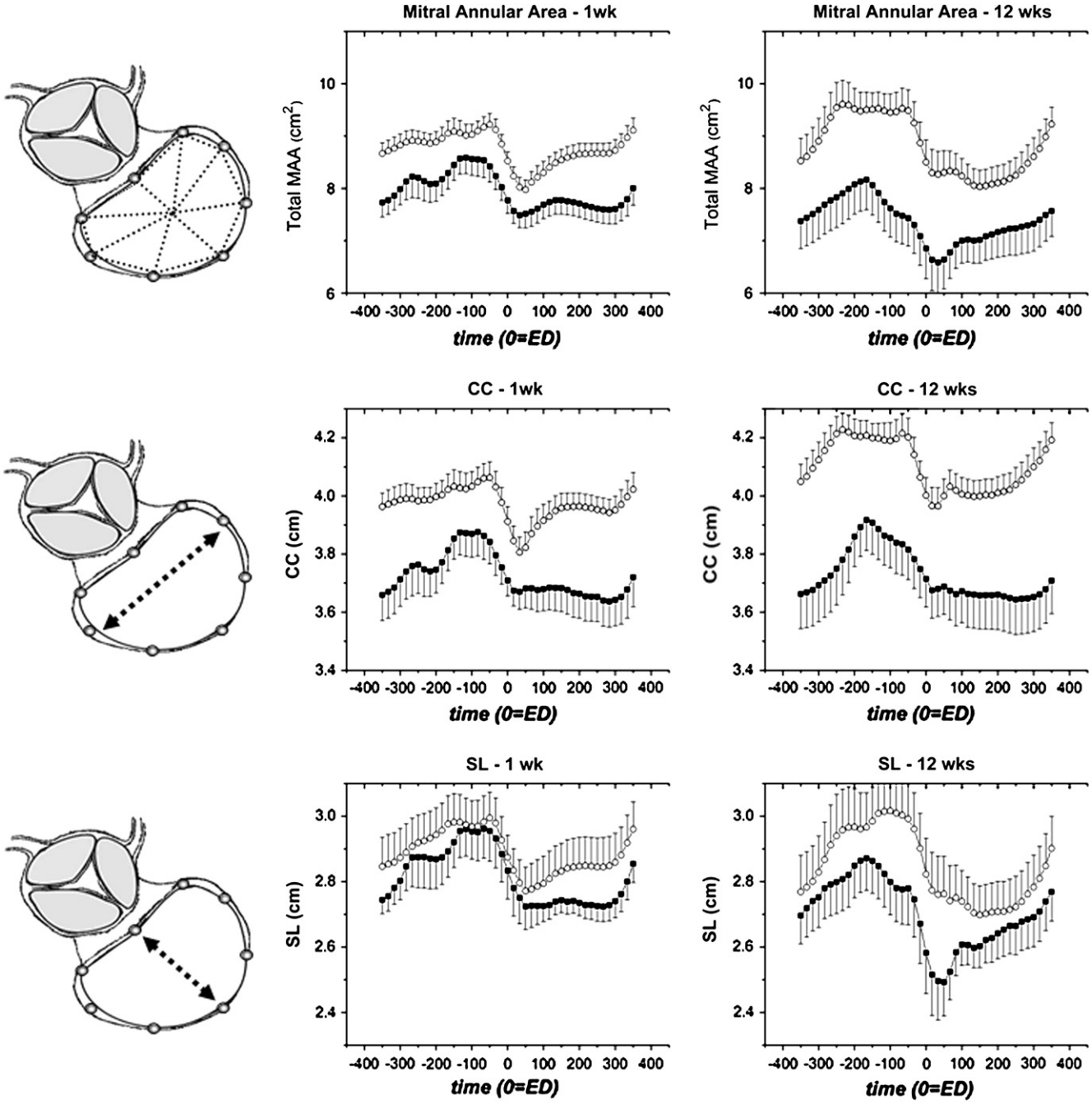

Figure 3. Comparison of mitral annular area, CC dimension, and SL dimension between CTRL (■, closed black squares) and HOLE (○, open circles) at both 1 week and 12 weeks throughout the cardiac cycle (mean ± 1 standard error of the mean). Data centered at ED ($t = 0$) in a 700-ms time window. *CC,* Commissure–commissure; *SL,* septal-lateral; *MAA,* mitral annular area.

regurgitant orifice area were not quantitatively measured; and (3) TTE in sheep is inherently difficult and the image quality may not be sufficient to discern subtle differences in MR grade. Despite these limitations, we believe it is important to qualify the concept "MR begets MR," because this situation may not necessarily hold true in the setting of pure low-pressure MR.

In this study, mitral annular area increased predominantly in the CC direction. It is thought, however, that perturbations in the mitral SL direction are more important

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TABLE 2. Annular geometry and shape

	1 wk			
	End diastole		End systole	
	CTRL	HOLE	CTRL	HOLE
MAA(i), cm^2/m^2	7.1 ± 0.8	8.1 ± 0.7[a]	5.8 ± 1.0	6.6 ± 0.9
CC(i), cm/m^2	3.2 ± 0.3	3.5 ± 0.4	2.9 ± 0.3	3.2 ± 0.4
SL(i), cm/m^2	2.4 ± 0.4	2.7 ± 0.3	2.3 ± 0.3	2.4 ± 0.3
	12 wk			
	End diastole		End systole	
	CTRL	HOLE	CTRL	HOLE
MAA(i), cm^2/m^2	6.8 ± 2.1	8.8 ± 1.3[a]	4.9 ± 1.8†	6.4 ± 1.1[a]
CC(i), cm/m^2	3.1 ± 0.5	3.8 ± 0.3[a,b]	2.8 ± 0.5	3.4 ± 0.3[a]
SL(i), cm/m^2	2.2 ± 0.5	2.5 ± 0.4[a]	1.8 ± 0.4	2.1 ± 0.3[a]

MAA(i), Mitral annular area indexed by BSA (cm^2/m^2); *CC(i),* commissure–commissure dimension indexed by BSA (cm/m^2); *SL(i),* septal-lateral dimension indexed by BSA (cm/m^2). Group mean (±standard deviation). [a]$P \leq .01$ versus CTRL. [b]$P \leq .04$ versus 1 week; Two-way repeated-measures analysis of variance with Bonferroni post hoc for multiple comparisons.

for leaflet coaptation compared with CC dilatation.[25,26] Annular dilatation alone may not be sufficient to support the "MR begets MR" supposition; understanding the regional dimensions of annular change is equally, if not more, important. Because SL dilation is known to predominate with chronic IMR, perhaps a more accurate description might be "chronic IMR begets more MR," although further studies are required to substantiate this possibility conclusively.

Annular 3-Dimensional Saddle Shape

The saddle-shape nonplanarity of the mitral annulus has been extensively described by 3D echocardiography, 4-dimensional marker videofluoroscopy, and sonomicrometry array localization.[27-30] By using finite element analysis, it is believed that the 3D annular saddle shape may be important for maintaining leaflet curvature that *pari passu* minimizes leaflet closing stress.[30] Annular 3D saddle shape, however, is not present in IMR, suggesting global flattening of the mitral annulus and, thus, a theoretic increase in leaflet stresses at ES.[4,24,31,32] It has been difficult to ascertain, however, whether the culprit of annular remodeling is the LV ischemic insult, the MR, or both. To isolate these variables, the mitral annular height and displacement of each annular marker from the mitral plane were measured in this chronic ovine model of pure MR without the confounding ischemia. There was no difference in mitral annular height throughout the cardiac cycle (Figure 4) between CTRL and HOLE at 12 weeks. To obtain a more complete picture of 3D annular geometry, the displacement of each annular marker from the mitral annular plane was calculated at ED and ES (Figure 5). There was no difference in marker displacement from the least-square annular plane between CTRL and HOLE at ED or ES. Furthermore, annular height to commissure-width ratio has been proposed as a normalized surrogate for annular 3D shape, and indeed this variable seems to be conserved across species.[4,30] Although end-systolic annular height to commissure-width ratio was smaller in HOLE versus CTRL at both 1 and 12 weeks, this difference was not significant (1 week: 10.3 ± 3.2 vs 12.1 ± 2.4; 12

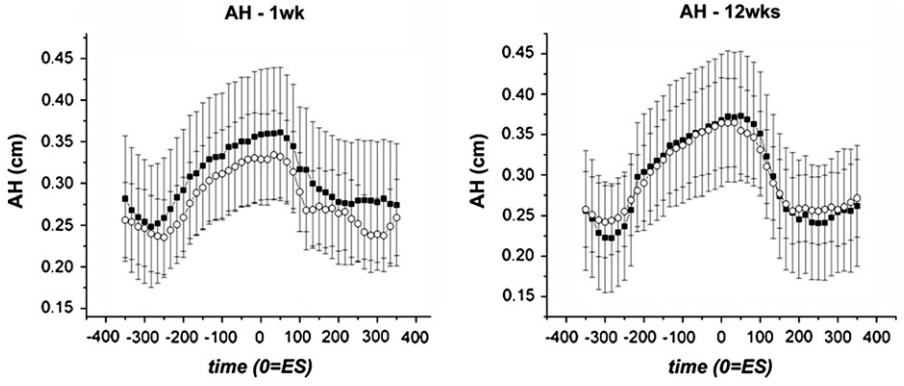

Figure 4. Mitral annular height between CTRL (■, closed black squares) and HOLE (○, open circles) at both 1 week and 12 weeks throughout the cardiac cycle (mean ± 1 standard error of the mean). Data centered at ES ($t = 0$) in a 700-ms time window. *AH,* Annular height; *ES,* end systole.

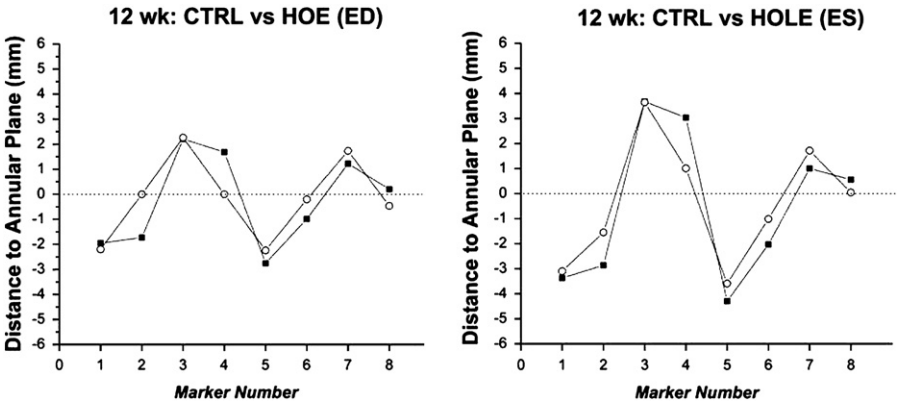

Figure 5. Distance of individual annular markers (1–8) at ED (*left*) and ES (*right*) from the least-squares annular plane for CTRL (■, closed black squares) versus HOLE (○, open circles) at 12 weeks. *ED,* End diastole; *ES,* end systole.

weeks: 10.6 ± 3.6 vs 13.0 ± 4.2, respectively, both not significant). These data, therefore, suggests that, in contrast with IMR, the 3D saddle shape of the mitral annulus does not flatten with pure MR. This implies that LV infarction plays the dominant role in annular flattening seen with chronic IMR. In both clinical and experimental studies, IMR is associated with a decrease in annular height,[4,31,32] whereas in this ovine study pure MR did not decrease annular height. It is known that the postinfarction remodeling associated with IMR results in lateral displacement of the posterior papillary muscle and LV wall.[3,33] Against a relatively fixed aortic annulus, lateral displacement of the ventricle could potentially "drag" the mitral annulus in the lateral direction, thereby flattening the mitral annulus (Figure 6), which might also explain why mitral annular SL dilation predominates in IMR, whereas it does not in pure MR dilation. Because pure MR did not alter the 3D saddle shape of the mitral annulus, theoretically, pure MR may have less of an effect on leaflet closing stress than does LV infarction, although this was not directly tested in this experiment.

Left Ventricular Remodeling

In this ovine experiment, there was only a minimal increase in LV ED volume despite 3+ MR in the HOLE group. MR is a chronic and insidious process that often takes years before substantial LV dilatation occurs; the relatively short duration of our study (12 weeks) probably accounts for the minimal increase in LV ED volume. Second, we support the supposition first introduced by the laboratory of Gorman and colleagues that infarction alone may play a more dominant role in LV remodeling than MR.[34-36] In previous IMR experiments by our and other groups, ventricular volume increased after the insult by 30% to 40% by 8 weeks. It was unclear from these previous studies, however, whether the increase was caused by the infarct, MR, or both. In this current study, we isolated the role of MR alone (without infarction). We conclude that MR causes LV dilatation, but at a slow and gradual rate, whereas infarction is more likely the major driving force responsible for adverse LV remodeling.

Conclusions

Considerable caution should be exercised when extrapolating results from this animal study to the clinical scenario of long-standing IMR or structural MR in humans. The sequela of MR is a chronic and insidious phenomenon that can be tolerated clinically for months to years. The 12-week follow-up in this study may be insufficient to capture the true pathophysiology of chronic MR. Although it is known that the amount of MR is heavily influenced by ventricular loading conditions, this variable was not directly controlled in this study.

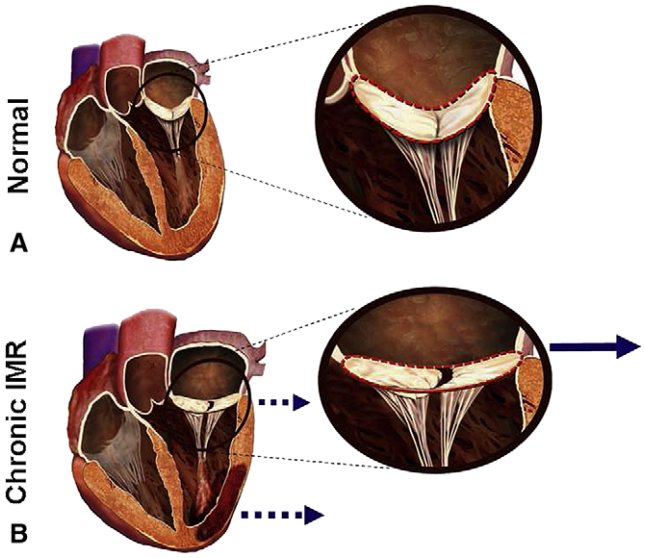

Figure 6. Cross-section of a normal (A) and chronic IMR heart (B) with schematic of the mitral annulus magnified on the right. Note that the mitral annulus (red dotted line) in the normal heart resembles the shape of saddle (A). After a posterior infarction, remodeling results in lateral displacement of the papillary muscle and ventricular wall (dotted blue line). Against a relatively fixed aortic annulus, this may "drag" the mitral annulus in the lateral direction thereby flattening the mitral annulus (solid blue line). This is also consistent with the predominant SL dilation seen with chronic IMR. *IMR,* Ischemic mitral regurgitation.

In future studies, however, we do plan to investigate how alterations in loading conditions affect annular geometry, dynamics, and annular 3D shape. Although we report that chronic pure MR did not alter mitral annular 3D saddle shape, it is possible that the study was not sufficiently powered to establish a statistical difference and that a type 2 (beta) error was made by incorrectly accepting the null hypothesis.

We appreciate the technical expertise provided by Lars Wigstrom, PhD, Frederick Tibayan, MD, Maggie Brophy, AS, Mary K. Zasio, BA, and Katha Gazda, BA. We thank Simon Kimm, MD, for the wonderful illustrations.

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Discussion

Dr Joseph H. Gorman *(Philadelphia, Penn).* That was a good talk, Tom. Another good study from your group.

I thought the most interesting aspect of this study was your ability—if you take your results in conjunction with the work that both your group and our group have done over the years studying ischemic MR in this model—you really, you get a sense of what the contribution of the MR is as compared to what the infarct effect is during the remodeling process that leads to heart failure. And if you looked at your data here, which is pure MR, the systolic volume increases by about 20% acutely and then really doesn't increase at all significantly over 12 weeks. If you look at this model when you give them a posterior infarct and they develop ischemic MR over 12 weeks, their ventricles may acutely increase by 30% or 40% and then they go on to increase in size by almost 3 times. So both of these models have the same amount of MR over the same amount of time, but the infarct model remodels much greater.

So that kind of gets at what we've been trying to point out over the last few years is that the ischemic MR, it's a ventricular disease, and it's the diseased ventricle that caused people to die. And potentially fixing the mitral valve doesn't impact much on survival, because it's not the driving force behind the remodeling.

Dr Nguyen. Thank you very much, Dr. Gorman, for your thoughtful comments on the presentation. I've learned a lot from your group's prolific contribution to the literature, and I feel very fortunate to have you as a discussant.

I've also followed very closely your group's position on MR and LV remodeling, specifically through recent publications (Guy et al., JACC 2004; Enomoto et al., JTCVS 2005; Enomoto et al., ATS 2005). Our data certainly does seem to suggest that infarction plays a more dominant role in LV remodeling than MR, at least in the limited 12-week time course of our study. To me, it's analogous to an explosion in the ventricle, an infarction versus the gradual force of MR. I suspect, though, that MR alone is probably still a factor in LV remodeling, albeit a slow and gradual one. But I think you're right that infarction is the total driving force.

I should probably also add that although we observed only a modest increase in ventricular remodeling—ventricular volumes, that is—I do believe that remodeling did occur evidenced by the significant difference in the left ventricular mass between control and hole at 12 weeks.

Dr Gorman. This study shows how well a normal ventricle can tolerate a big volume load. It doesn't increase in size, but it hypertrophies effectively to handle the volume load.

I just have a second comment. I don't totally agree with the conclusion of this study that the data supports the need for disease-specific rings. It's always been my bias that in much of valve repair that a ring should try to re-establish as near a normal annular shape as possible, and that's along the lines of the work we've done with the saddle ring. And I think whether you're treating ischemic MR or you're treating xanthomatous disease, I think your repair is best served if you try to either maintain or re-establish that more normal shape.

Dr Nguyen. I completely agree with you that surgical strategies should be directed at maintaining annular 3D saddle shape. Too bad there's not a way to personalize annuloplasty rings according to a person's unique 3D saddle shape, perhaps by a preoperative 3D echo matched to the appropriate 3D annuloplasty ring. That said, for IMR, there still might be a role for rings that disproportionately reduce the SL dimension, since this helps address perturbations in subvalvular geometry, specifically papillary muscle displacement.

Furthermore, Maisano et al. (ATS 2005) demonstrated in a finite element model that dog bone rings were less affected by papillary muscle displacement than traditional D-shaped rings.

With respect to pure MR, I am not sure if from my study I would advocate a ring that disproportionately reduced the CC dimension—and, as you mentioned, I think that restoring natural 3D annular shape is probably more important.