Mechanistic Insights Into Posterior Mitral Leaflet Inter-Scallop Malcoaptation During Acute Ischemic Mitral Regurgitation

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Background—Three-dimensional dynamics of the 3 individual scallops within the posterior mitral leaflet during acute ischemic mitral regurgitations have not been previously measured.

Methods—Radiopaque markers were sutured to the mitral annulus, papillary muscle tips, and leaflet edges in 13 sheep. Immediately postoperatively, under open-chest conditions, 3-D marker coordinates were obtained using high-speed biplane videofluoroscopy before and during echocardiographically verified acute ischemic mitral regurgitation produced by occlusion of the left circumflex coronary artery.

Results—During acute ischemic mitral regurgitation, at end systole, the anterolateral edge of the central scallop was displaced 0.8±0.9 mm laterally and 0.9±0.6 mm apically away from the anterolateral scallop; such displacement correlated with lateral displacement of the lateral annulus (R²=0.7, SEE=0.7 mm, P<0.001) and movement of the right lateral annulus away from the nonischemic anterior papillary tip (R²=0.6, SEE=0.8 mm, P=0.002), respectively. End-systolic displacement of the posteromedial edge of the central scallop was 1.4±0.9 mm anteriorly and 0.9±0.6 mm laterally away from the postero medial scallop, corresponding to anterior displacement of the mid-lateral annulus (R²=0.5, SEE=1.0 mm, P<0.001).

Conclusions—Malcoaptation of the scallops within the posterior leaflet during acute left ventricular ischemia is a novel observation. The primary geometric mechanism underlying scallop malcoaptation in acute ischemic mitral regurgitation was annular dilatation, which hindered leaflet coaptation by drawing the individual scallops apart. These findings support the use of annular reduction in the repair of ischemic mitral regurgitation and also suture closure of prominent subcommissures between posterior leaflet scallops. (Circulation. 2002;106[suppl I]:I-40-I-45.)

Key Words: Ischemic mitral regurgitation ■ mitral valve 3-D geometry ■ leaflet dynamics ■ posterior mitral leaflet ■ mitral scallops ■ ischemic heart disease ■ coronary artery disease

Mitral valve repair has traditionally focused on restoring coaptation of the anterior and posterior mitral leaflets in patients with ischemic mitral regurgitation (MR), where various types of leaflet malpositioning can occur, as detailed in Carpentier’s classification scheme. The posterior mitral leaflet, unlike the anterior leaflet, is typically divided into 3 scallops by subcommissures along its free margin. In 2000, T. Myrmel observed that malcoaptation of these scallops within the posterior leaflet may contribute to ischemic MR. This phenomenon of scallop malcoaptation is not widely recognized, and little attention has been paid to posterior leaflet inter-scallop coaptation during mitral valve repair; thus, we reasoned that better understanding of inter-scallop coaptation might have therapeutic implications for surgical mitral repair in patients with ischemic MR. The present experiment was designed to provide more knowledge of 3-D dynamic motion of the scallops within the posterior mitral leaflet and inter-scallop coaptation during acute LV ischemia.

Methods

Glossary:

MR = Mitral regurgitation
P = Anterolateral scallop of the posterior leaflet
Pac = Portion of the central scallop of the posterior leaflet that coapts with P
Ppc = Postero medial scallop of the posterior leaflet
Pac = Portion of the central scallop of the posterior leaflet that coapts with P
Aanterior = Anterior mitral leaflet near the anterior commissure
Aposterior = Anterior mitral leaflet near the posterior commissure

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Figure 1. Details of the marker array used for the mitral annulus and leaflets. Markers were sutured to the mid-septal annulus (#1), left fibrous trigone (#2), anterior commissure (#3), left lateral annulus (#4), mid-lateral annulus (#5), right lateral annulus (#6), posterior commissure (#7) and right fibrous trigone (#8). Markers were sutured to the edges of the anterior mitral leaflet (Aantom; Aantcom; Aanteam; Aac; Aapcom; Apcom), that coapt with the anterolateral scallop (P a); anterolateral central scallop (P ac); posteromedial portion of the central scallop (Ppc) and posteromedial scallop (P p). Markers (#1), left fibrous trigone (#2), anterior commissure (#3), left lateral annulus (#4), mid-lateral annulus (#5), right lateral annulus (#6), posterior commissure (#7) and right fibrous trigone (#8).

LV = left ventricle

Surgical Preparation

Miniature radiopaque markers were surgically implanted in 13 adult castrated male sheep with a mean body weight of 72±9 kg. A dense leaflet marker array was designed to elucidate the 3-D scallop dynamics of the mitral valve. General technical details have been described before and are only briefly summarized here. After establishing cardiopulmonary bypass, the mitral annulus was delineated with 8 markers (Figure 1). Markers were also placed at the tips of the anterior and posterior papillary muscles, and sutured to the mitral leaflet edges as depicted in Figure 1. Leaflet marker nomenclature X, was based on anatomical position with “X” specifying the leaflet (A = Anterior; P = Posterior) and “y” the marker location on the leaflet (acom = near the anterior commissure; pcom = near the posterior commissure; a = anterolateral scallop; ac = anterolateral portion of the central scallop; pc = posteromedial portion of the central scallop; p = posteromedial scallop).

Experimental Protocol

Immediately postoperatively with the chest open, each animal was placed in the right lateral decubitus position and mechanically ventilated with 100% oxygen and anesthetized. Simultaneous biplane videofluoroscopic and hemodynamic data were acquired before and during ischemia. Animals were studied in normal sinus rhythm with ventilation arrested at end-expiration for a few beats during data acquisition runs to minimize the effects of respiration. To create acute posterolateral LV ischemia, the left circumflex coronary artery was occluded proximal to the first obtuse marginal artery by cinching an encircling suture. Before and following 2 to 3 minutes of ischemia, data were acquired at 60 Hz in the 7-inch mode of image magnification and two-dimensional images from each of the 2 x-ray views were digitized and merged to yield 3-D coordinates every 16.7 ms using custom designed software. Mitral regurgitation was graded from transesophageal color Doppler echocardiography by an experienced echocardiographer as none to trace (grade 0), mild (grade 1), moderate (grade 2) or severe (grade 3). 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 [NIH] Publication 85 to 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 Analysis

Data from 2 consecutive steady-state beats during control and acute ischemic conditions were averaged and analyzed. End-systole was defined as the videofluoroscopic frame immediately preceding the peak negative rate of LV pressure change (-dP/dtmax), and end-diastole was defined as the videofluoroscopic frame containing the peak of the R-wave on the ECG. All dimensional data reported herein were measured at the time of end-systole.

Internal Coordinate Reference System and Geometric Variables

At each sample time, a mitral annular plane was defined by least-squares fit to the 3-D coordinates of 7 of the 8 mitral annular markers (#2 to 8, Figure 1), omitting the mid-septal annular marker #1 (Figure 1) which as the “saddle horn” lies above the mitral annular plane. The origin of a right-handed internal coordinate system was defined by the projection of the right fibrous trigone annular marker (#8, Figures 1 and 2) onto this plane. The positive x-axis passed anteriorly through the projection of the left fibrous trigone annular marker (#2, Figures 1 and 2) onto this annular plane. The positive y-axis was located in the mitral annular plane, orthogonal to the x-axis and directed toward the lateral annulus. The positive z-axis was oriented orthogonal to the mitral annular plane, and directed toward the left atrium (Figure 2).

The origin of the reference system was translated to Pp to simplify interpretation of Pp – Pp coaptation (ie, position of Pp relative to Pp). Similarly, the origin was translated to Pp to study Pp – Pp coaptation. Using these coordinate systems, displacements were defined as the change in end-systolic position of each marker during LV ischemia relative to its nonischemic position. The following measurements were computed from 3-D marker coordinates before and during ischemia at end-systole: Inter-scallop distances, inter-leaflet distances, distances between the papillary tips and the lateral annular markers, lateral annular segmental lengths, and septal-lateral and commissure-comissure annular dimen-
sions. These distances are independent of the coordinate system chosen.

**Statistical Analysis**

All results are reported as mean ±1 SD. The geometric variables measured before and during ischemia at end-systole were compared using a two-tailed Student’s t test for paired observations. The 3-D geometry of the mitral leaflets is ultimately governed by the material properties of the leaflets and the 3-D geometry of the structures attached to the leaflets, that is, mitral annulus and papillary muscle tips. Thus, any change in the 3-D geometry of the mitral annulus and papillary muscle tips during acute LV ischemia will produce changes in leaflet geometry that could lead to ischemic MR.

To determine the changes in annular and papillary muscle tip geometry most closely associated with specific changes in observed leaflet geometry, we used a multivariable statistical model with leaflet geometry change as the dependent variable and changes in annular and papillary muscle tip geometry the independent variables. A stepwise linear regression model (SPSS for Windows, Release 10.0.0, SPSS Inc., Chicago, IL) was used to identify predictors of leaflet geometry change, that is, change in 3-D scallop geometry. The aim of the multivariable analysis was to determine which component of the annular and papillary muscle tip geometry was most important with respect to a specific change in leaflet geometry. Such statistical analysis sheds light on the geometric mechanisms underlying changes in leaflet geometry and consequently ischemic MR.

**Results**

Post-mortem examination revealed that all 8 mitral annular markers were within 1 mm of the mitral leaflet- left atrial junction in all animals.

**Mitral Valve Competence**

Of the 13 animals, mild baseline MR was observed in 4, trace MR in 8 and no MR in 1 before ischemia. After 2 to 3 minutes of ischemia, the 4 animals with mild MR developed moderate (n=2) or severe (n=2) holosystolic MR, and the other 9 animals developed mild (n=3), moderate (n=3), or severe (n=3) MR. Overall, MR increased from an average grade of 0.3 at baseline to a grade of 2.2 (P<0.001) during acute LV ischemia. We could not determine precisely the specific location of the MR jet, but it was broadly central.

**Hemodynamics**

The acute ischemic injury was substantial, producing a 38% decrease in LV dp/dtmax (from 1,860±471 mm Hg/s to 1,149±227 mm Hg/s, P<0.001), a 37% drop in end-systolic LV pressure (from 92±17 mm Hg to 63±11 mm Hg, P<0.001), a 26% decrease in maximal LV pressure (from 112±9 mm Hg to 83±8 mm Hg, P<0.001), and a 37% increase in end-diastolic LV pressure (from 18±5 mm Hg to 24±5 mm Hg, P<0.001). There was no significant change in heart rate (94±10 bpm versus 91±14 bpm respectively).

**Inter-Scallop Malcoaptation**

As shown in Figure 3, the scallops of the posterior mitral leaflet moved apart at end systole during LV ischemia: Pa –

**Inter-leaflet Malcoaptation**

The acute and posterior leaflets also moved apart during acute LV ischemia: Aacom – Pa, Apcm – Pp, and Apcm – Pp distances increased by 0.9±0.9 mm (P=0.002), 2.5±1.4 mm (P<0.001) and 1.4±0.9 mm anteriorly (P<0.001) away from Pp, producing inter-scallop separation and restriction. Pp was displaced 0.9±0.6 mm laterally (P<0.001) and 1.4±0.9 mm anteriorly (P<0.001) away from Pp, producing inter-scallop separation in the septal-lateral and anterior-posterior (inter-commisural) direction (Figure 4B).

**Mitral Annulus**

During acute LV ischemia, the septal-lateral (from marker 1 to marker 5, Figure 1) and commissure-commissure (from marker 3 to marker 7, Figure 1) annular dimensions increased by 5.0±3.3 mm (30.2±9.4 to 35.2±13.5 mm, P<0.001) and 2.6±1.7 mm (39.2±8.8 to 41.6±9.0 mm, P<0.001), respectively. Figure 3 depicts the significant changes with LV ischemia in lateral annular dimensions at end-systole which increased by 1.1±1.2 mm (11.1±1.5 mm to 12.4±2.0 mm, P=0.007) between the anterior commissure (marker 3) and the left lateral annulus (marker 4), 2.0±1.3 mm (13.1±3.2 mm to 15.1±0.4 mm, P<0.001) between the left lateral (marker 4) and mid-lateral annulus (marker 5), 1.8±1.0 mm (18.7±6.5 mm to 20.4±5.8 mm, P<0.001) between the mid-lateral (marker 5) and right lateral annulus (marker 6) and 3.8±2.3 mm (15.5±4.6 mm to 19.1±7.6 mm, P<0.001) between the right lateral annulus (marker 6) and posterior commissure (marker 7). Statistically significant displacements of the lateral annulus relative to Pp are depicted graphically in Figure 4A, and those relative to Pa are shown in Figure 4B. The septal annular distance between the fibrous trigones (markers 2 to 1 to 8) did not change significantly during acute LV ischemia (25.6±7.5 versus 25.9±8.0, P=0.13).

**Papillary Muscle Tips**

Statistically significant end-systolic displacements of the anterior papillary muscle tip relative to Pa and the posterior
papillary tip relative to Pp during LV ischemia are depicted in Figures 4A and 4B, respectively.

**Annular-Papillary Distances**

During LV ischemia, the distances between the tip of the nonischemic anterior papillary muscle and each of the lateral annular marker sites increased (Table 1), particularly that to the right lateral annulus. The distance between the ischemic posterior papillary tip and both the right lateral and mid-lateral annulus did not change during ischemia, while the distance between the posterior papillary tip and the left lateral annulus increased during ischemia (Table 1).

**Predictors of Inter-Scallop Malcoaptation From Stepwise Linear Regression**

During acute ischemic MR, Pac was displaced 0.8 mm laterally, drawn by the 2.2 mm lateral displacement of the mid-lateral annulus ($R^2=0.7$, SEE=0.7 mm, $P<0.001$) (Refer to Figures 4A and 4B). A 3.7 mm movement of the anterior papillary muscle tip away from the right lateral annulus predicted PAc restriction of 0.9 mm ($R^2=0.6$, SEE=0.8 mm, $P=0.002$). Ppc was displaced 1.4 mm anteriorly and 0.9 mm away from Pp, drawn by the 3.1 mm anterior displacement of the mid-lateral annulus ($R^2=0.5$, SEE=1.0, $P<0.001$).

**Discussion**

Separation of the Pp - Ppc and Pp - Pac posterior leaflet scallops is a novel observation that has hitherto not been reported during acute LV ischemia. The similar magnitude of inter-scallop and anterior-posterior mitral leaflet separation indicates that inter-scallop separation may contribute significantly to the effective regurgitant orifice (ERO) area in acute ischemic MR. Importantly, postinfarction mortality is directly related to the severity of ischemic MR as measured by the ERO area and regurgitant volume.7

Three-dimensional analysis demonstrated that:

1. Pac was displaced laterally and apically (restriction) away from Pa (Figure 4A);
2. Ppc was displaced anteriorly and laterally away from Pp (Figure 4B);
3. Separation of all 3 scallops occurred predominantly in directions parallel to the annular plane, and that inter-scallop separation in a direction perpendicular to the annular plane (ie, apical tethering or restriction) was relatively less important, being seen in 2 of the 3 scallops (Pac and Pp); and,
4. Perturbations of scallop geometry were heterogeneous and complex in nature, being different in each scallop. Attention to these individual changes in scallop geometry may be important in mitral valve repair for ischemic MR.

By correlating 3-D perturbations of mitral annular and papillary muscle tip geometry in a multivariable linear regression model, this study showed that annular-papillary displacement was responsible for scallop restriction (inter-scallop separation perpendicular to the annular plane). To illustrate the mechanism, one can imagine a length of rope running from the anterior papillary tip to Pac and then bending toward the...
right lateral annulus (marker #6). As the right lateral annulus is displaced away from the nonischemic anterior papillary tip, the rope is straightened, and \( P_{\text{nc}} \) is drawn down into the LV cavity toward the LV apex. In contrast, displacement of left lateral annulus away from the posterior papillary tip did, however, not produce \( P_{\text{pc}} \) restriction because of movement of the ischemic posterior papillary muscle tip toward the annular plane, which tended to prolapse \( P_{\text{pc}} \).

The multivariable model also demonstrated that the scallops were drawn apart in directions parallel to the annular plane by dilatation of the mitral annulus. Thus, septal-lateral annular dilatation drew \( P_{\text{nc}} \) laterally away from \( P_{\text{a}} \) (Figure 4A). An increase in lateral annular dimensions also correlated with anterior and lateral displacement of \( P_{\text{pc}} \) away from \( P_{\text{p}} \) (Figure 4B). To explain the unexpected lateral displacement of \( P_{\text{pc}} \), one can imagine a length of rope running from the mid-lateral annulus (marker #5) to \( P_{\text{pc}} \) and bending toward the right lateral annulus (marker #6). As the mid-lateral annulus moves anteriorly away from the right lateral annulus, the bend in the rope straightens which displaces \( P_{\text{pc}} \) laterally and also anteriorly away from \( P_{\text{p}} \).

Separation of scallops parallel to the annular plane occurred in all 3 scallops, whereas scallop separation perpendicular to the annular plane was seen in only 2 of 3 scallops (\( P_{\text{nc}} \) and \( P_{\text{p}} \)). Thus, we surmised that mitral annular dilatation (responsible for scallop separation parallel to the annular plane) was relatively more important than annular-papillary displacement (responsible for scallop separation perpendicular to the annular plane) in the pathogenesis of scallop malcoaptation during acute LV ischemia.

**Clinical Inferences**

This present experiment indicates that ring annuloplasty could help to restore coaptation of all 3 scallops of the posterior leaflet during ischemic MR by preventing septal-lateral annular dilatation and elongation of the lateral annulus. There is one major caveat as the finding of inter-scallop malcoaptation in this acute ischemic ovine model cannot be extrapolated to patients with chronic ischemic MR where LV dilatation and remodeling play a greater role than annular dilatation. Furthermore, there is no evidence that inter-scallop malcoaptation occurs in chronic ischemic MR. Nevertheless, one of us (D. Liang) has verified echocardiographically the presence of chronic ischemic MR jets originating from the junction of the posteromeral and central scallops (Figure 5) in patients with Carpentier type IIIb (restricted systolic) posterior leaflet motion. Demonstration of inter-scallop malcoaptation in this experimental model may lend weight to the surgical practice of suture closure of prominent subcommisures between any 2 well-developed scallops of the posterior leaflet.
leaflet when undertaking mitral repair for ischemic MR. Such well differentiated scallops and deep subcommissures are generally associated with patients who have myxomatous valve disease, but also can be a normal variant.

Limitations
The interpretation of 3-D data are dependent on the frame of reference. The advantages of using the mitral annular plane as a frame of reference have been previously discussed. Caution should obviously be exercised in extrapolating the findings in this acute ischemic open-chest ovine model to patients with chronic ischemic MR. Apart from the end-systolic data presented here, these data were analyzed at other systolic time points (defined by 25%, 50% and 75% ejection of LV volume) which verified that the inter-scallop malcoaptation described here was truly a pansystolic phenomenon consistent with holosystolic MR. The TEE-visualized MR jet was broadly central in location, thus it could not be determined precisely whether the MR jet had arisen from the region of scallop separation. The radiopaque marker method requires suturing small metal markers to the leaflets, but it is unlikely that the markers interfered with mitral leaflet motion, as they are quite small (aggregate mass = 20±6 mg). Finally, while this study addressed the geometric changes in the mitral valve that occurred during occlusion of the proximal (dominant) circumflex artery, we have no data on perturbations of mitral valve geometry that might arise with ischemia in different LV regions and of varying duration.

Conclusions
Malcoaptation of the scallops within the posterior leaflet during acute LV ischemia is a new observation that may have potential therapeutic implications for repair of ischemic MR. In this model, the primary geometric mechanism underlying scallop malcoaptation in acute ischemic MR was annular dilatation, which hindered leaflet coaptation by drawing the individual scallops apart. Inter-scallop apical restriction also played a role in scallop malcoaptation. These findings support the use of annular reduction procedures in the repair of ischemic MR and the practice of suture closure of prominent subcommissures between posterior leaflet scallops.

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