Will a Partial Posterior Annuloplasty Ring Prevent Acute Ischemic Mitral Regurgitation?

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Background—Acute posterolateral ischemia in sheep results in ischemic mitral regurgitation (IMR). While complete ring annuloplasty prevents acute IMR, partial annuloplasty rings may offer a more physiologic repair, but are untested in animal models of IMR.

Methods—Radioopaque markers were placed on the LV, mitral annulus (MA), and leaflets in 13 sheep. Seven sheep served as controls, and 6 had a St. Jude Tailor partial flexible ring implanted (29 mm in 5, 31 mm in 1). After 8 ± 1 day, the animals were studied with biplane videofluoroscopy and echocardiography before and during acute posterolateral LV ischemia (balloon occlusion of circumflex artery). Mitral annular area (MAA), septal-lateral annular diameter (SL), annular perimeters, and leaflet edge separation were calculated from 3-D marker coordinates.

Results—The average degree of mitral regurgitation increased from 0.0 ± 0.0 to 2.1 ± 0.7 (P = 0.0006) in the control group during acute ischemia but remained unchanged in the Tailor group (0.1 ± 0.2 for both conditions). The change in MAA throughout the cardiac cycle before ischemia was 17 ± 4% in control animals, but only 5 ± 2% (P = 0.0002) in the Tailor ring group. Unlike the control animals, there was no increase in MAA (5.4 ± 0.8 and 5.5 ± 0.7 cm², respectively; p = NS) nor dilatation of the muscular annulus (6.2 ± 0.3 and 6.2 ± 0.4, respectively; p = NS) during ischemia with the Tailor ring. Mitral SL dimension increased slightly with ischemia (2.3 ± 0.2 versus 2.2 ± 0.2 cm, P = 0.03). Although posterior leaflet motion was limited, as observed with complete rings, normal annular flexion was maintained with the Tailor ring before and during acute ischemia.

Conclusions—The Tailor partial annuloplasty ring prevented acute IMR probably by limiting SL diameter dilatation during acute ischemia. In this animal model of acute IMR, a partial, flexible posterior annuloplasty ring is as effective as a complete ring. (Circulation. 2002;106[suppl I]:I-33-I-39.)

Key Words: ischemia ▪ mitral valve ▪ regurgitation ▪ valvuloplasty
Figure 1. Array of ventricular (dark circles), annular (light circles), and leaflet (squares) markers used in the study. AML = anterior mitral leaflet; PML = posterior mitral leaflet.

Methods

Surgical Preparation

Thirteen adult sheep were used in the study. The operative procedure for marker implantation has been described previously in detail. The markers were implanted on the left ventricle, around the mitral annulus, and on the central meridian of each leaflet as shown in Figure 1. On cardiopulmonary bypass via a left atriotomy, the mitral valve was sized using both the distance between the fibrous trigones and the area of the anterior leaflet, and an appropriately sized Tailor ring was implanted (5 animals received a 29 mm ring, and 1 a 31 mm ring) using 8 to 10 interrupted horizontal mattress sutures of 2-0 braided Dacron. A micromanometer pressure transducer (PA4.5-X6; Konigsberg Instruments, Inc, Pasadena, CA) was placed in the LV chamber through the apex, and pneumatic occluders were placed around the superior and inferior vena cava after the animals were weaned from cardiopulmonary bypass. Seven animals underwent marker implantation only and served as a control group. The annular and leaflet dynamics in this historical control group have been reported. All animals were recovered in the experimental animal care facility during the first postoperative day.

Data Acquisition

The animals were studied during closed-chest conditions, sedated with ketamine and diazepam, intubated and mechanically ventilated (veterinary anesthesia ventilator 2000, Hallowell EMC) with 100% oxygen. Esmolol (20 to 50 μg/kg/min) and atropine sulfate (0.01 mg/kg/min) intravenous infusions were utilized to minimize reflex sympathetic and parasympathetic responses. Left circumflex coronary balloon occlusion (distal to the first obtuse marginal artery) to produce posterolateral LV ischemia was carried out. Simultaneous biplane videofluoroscopy and hemodynamic data recordings were obtained during steady-state conditions and over a range of LV filling volumes during abrupt preload reduction using vena caval occluders. Data recordings were acquired before and after balloon circumflex occlusion. Resultant IMR was graded subjectively by an experienced echocardiographer (D. Liang) according to the extent and width of the regurgitant jet and categorized as none (0), mild (+1), moderate (+2), moderate to severe (+3), or severe (+4).

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 Animal Review committee and conducted according to Stanford University policy.

A Philips Optimus 2000 biplane Lateral ARC 2/poly DIAGNOST C2 system (Philips Medical Systems, North America Company) was used to record videofluoroscopic data at 60 Hz with the image intensifiers in the 9-inch mode. Two-dimensional images obtained from each of the 2 x-ray views (45° right anterior oblique and 45° left anterior oblique) were digitized and then merged to yield 3-D coordinates for each marker every 16.7 ms. LV pressure, aortic pressure, and ECG voltage were digitized and recorded simultaneously.

Data Analysis

End-systole was defined as the videofluoroscopic frame preceding maximum negative dP/dt (-dP/dt max); end-diastole was defined as the videofluoroscopic frame containing the peak of the ECG R-wave. An instantaneous estimate of LV volume was calculated every 16.7 msec from the epicardial LV markers using a multiple tetrahedral model reconstructed from the marker coordinates. External LV pressure-volume stroke work (SW) was calculated as the integral of LV pressure (P) on volume (V) over a cardiac cycle for several beats at baseline and during caval occlusion as:

\[ SW = \int P \, dV \]

Preload recruitable stroke work (PRSW) was computed by linear regression of SW on EDV as:

\[ SW = MW \times (EDV - VW) \]

Where MW and VW are the slope and volume axis intercept, respectively. Adequate volume occlusion for PRSW calculations was obtained in 6 animals for the control and 4 animals in the Tailor groups.

Mitral Annular Geometry

Mitral annular area, perimeters, and dimensions where computed from the 3-D marker coordinates without assuming circular or planar...
Figure 3. Group mean data for muscular annular perimeter (top panel), fibrous annular perimeter (middle panel), and total annular perimeter (bottom panel) throughout the cardiac cycle for control (left) and Tailor (right) groups before (closed symbols) and during (open symbols) acute posterolateral ischemia. A 650 ms time interval centered at end-diastole (t=0) is illustrated for both groups. Error bars represent ±1 SEM.
Mitral Leaflet Dynamics
To assess leaflet mobility throughout the cardiac cycle, angular position of the anterior leaflet edge was calculated as the angle (ΘAML) between the line from the anterior leaflet edge marker to the "saddle horn" and the septal-lateral annular diameter. Posterior leaflet edge angular position (ΘPML) was calculated in similar fashion. Leaflet excursion was calculated from diastolic maximum to systolic minimum angle. Anterior and posterior leaflet lengths were measured as the sum of distances between adjacent markers placed on the central meridian of each leaflet. Leaflet edge separation was determined as the distance in 3-D space between the 2 edge markers on the anterior and posterior mitral leaflets with valve closure defined as the time at which this distance reached its minimum plateau. Because of loss of the marker on the anterior leaflet edge in some animals, leaflet separation distance was calculated in 5 control and 4 Tailor animals.

Statistical Analysis
All data are reported as mean plus or minus 1 standard deviation (±1 SD). Hemodynamic and marker-derived data from 2 to 3 consecutive steady state beats that were time-aligned at end-diastole, and data from these beats were averaged for each animal. The data were analyzed for 20 frames before and 20 frames after end-diastole. Data were compared using Student’s t test for paired comparisons.

Results
Hemodynamics
The animals in the Tailor group were larger than those in the control group (77±9 kg versus 63±9 kg; P=0.02); additionally, they had longer cardiopulmonary bypass (171±21 versus 94±18 minute; P=0.0001) and aortic cross clamp (117±17 versus 65±24 minute) times. Group mean hemodynamic parameters before and after induction of acute posterolateral LV ischemia in each group are shown in Table 1. Before ischemia, the 2 groups were comparable in all hemodynamic parameters except end-systolic volume was greater in the Tailor group and the control animals had a higher baseline LV dP/dt. Peak and end-systolic LV pressures decreased while LV end-systolic volume increased in both groups with proximal circumflex occlusion. Furthermore, preload recruitable stroke work (PRSW), a load independent index of LV function, fell a similar degree in both groups during circumflex occlusion suggesting an equivalent ischemic insult. During acute IMR, mitral regurgitation increased from none to moderate in the control group, but remained only trace in the Tailor group.

Mitral Annular Dynamics
Group mean data for mitral annular area and SL and CC diameters as well as lengths of the fibrous and muscular portions of the mitral annulus are tabulated in Table 2 and shown in Figures 3 and 4. During acute posterolateral ischemia in the control group, the mitral annulus (particularly in the SL diameter) dilated substantially, and the length of the muscular annular perimeter increased significantly. Conversely, during circumflex occlusion in the Tailor group, annular area did not change, and there was no appreciable increase in either the SL diameter or the muscular annular perimeter. Mitral annular area changed only slightly during the cardiac cycle before and during ischemia in the animals fitted with the partial flexible annuloplasty ring. Although annular area remained fixed in the Tailor group, flexion of the septal annulus, as shown in Figure 5, was similar in both groups before ischemia (1.9±0.9 and 1.5±0.3 mm for control

Figure 4. Group mean data for mitral annular area (top panel), SL dimension (middle panel), and CC dimension (bottom panel) throughout the cardiac cycle for control (left) and Tailor (right) groups before (closed symbols) and during (open symbols) acute posterolateral ischemia. A 650 ms time interval centered at end-diastole (t=0) is illustrated for both groups. Error bars represent ±1 SEM.
were effective in preventing acute IMR, but ring implanta-
tions perturbed annular and leaflet dynamics. Recent reports have claimed preserved annular motion with a partial flexible posterior annuloplasty ring in human subjects hence offering hope for a more physiologic repair. The data in the current experiment demonstrated that the Tailor partial flexible annuloplasty ring was effective in preventing acute IMR in otherwise normal sheep hearts; no increase in annular septal-lateral dimension nor dilatation of the muscular annulus was observed. Unexpectedly, this partial ring also abol-
ished left ventricular (LV) remodeling and function in a clinical setting.

**TABLE 3. Leaflet Angular Motion, Closure Timing, and Lengths**

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Tailor</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pre-ischemia</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AML&lt;sub&gt;EXC&lt;/sub&gt; (°)</td>
<td>45±12</td>
<td>38±16</td>
</tr>
<tr>
<td>PML&lt;sub&gt;EXC&lt;/sub&gt; (°)</td>
<td>38±3</td>
<td>32±4*</td>
</tr>
<tr>
<td>Valve closure (ms)</td>
<td>17±4</td>
<td>84±12*</td>
</tr>
<tr>
<td>AML-Length&lt;sub&gt;ES&lt;/sub&gt; (cm)</td>
<td>2.08±0.13</td>
<td>2.19±0.09*</td>
</tr>
<tr>
<td>PML-Length&lt;sub&gt;ES&lt;/sub&gt; (cm)</td>
<td>1.33±0.17</td>
<td>1.33±0.17*</td>
</tr>
<tr>
<td><strong>Ischemia</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AML&lt;sub&gt;EXC&lt;/sub&gt; (°)</td>
<td>38±10</td>
<td>46±10</td>
</tr>
<tr>
<td>PML&lt;sub&gt;EXC&lt;/sub&gt; (°)</td>
<td>14±6†</td>
<td>15±6</td>
</tr>
<tr>
<td>Valve closure (ms)</td>
<td>67±13</td>
<td>72±25</td>
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<tr>
<td>AML-Length&lt;sub&gt;ES&lt;/sub&gt; (cm)</td>
<td>2.08±0.37</td>
<td>2.11±0.34</td>
</tr>
<tr>
<td>PML-Length&lt;sub&gt;ES&lt;/sub&gt; (cm)</td>
<td>1.03±0.17</td>
<td>1.00±0.20</td>
</tr>
</tbody>
</table>

*P<0.05 versus pre-ischemia by t test for paired observations; †P<0.05 pre-ischemia Tailor versus pre-ischemia control (data for anterior leaflet length and excursion and valve closure time derived from 5 animals in the control group and four animals in the Tailor group).

**Discussion**

Currently, ring annuloplasty represents the mainstay of surgical therapy in correcting ischemic mitral regurgitation although it is not universally effective. In prior experimental studies, complete flexible and semi-rigid annuloplasty rings were effective in preventing acute IMR, but ring implanta-

**Mitral Leaflet Dynamics**

Group mean anterior and posterior leaflet edge angular positions during the cardiac cycle for both groups before ischemia are illustrated in Figure 6. Anterior leaflet excursion from minimum to maximum during the cardiac cycle was similar between the 2 groups (45±12 and 50±10 degrees for control and Tailor, respectively; P=0.5), posterior leaflet motion was severely limited in the Tailor group (38±3 versus 14±7 degrees; P=0.0001). Changes in leaflet excursion in both groups during ischemia along with valve closure times and lengths of the anterior and posterior leaflets at end-systole are summarized in Table 3. During circumflex occlusion, posterior leaflet excursion decreased in control animals but did not change in the Tailor group. The observed mitral regurgitation in the control group was associated with delayed valve closure and early systolic leaflet “loitering” (Figure 7). In the Tailor group, although there was a trend toward later valve closure at baseline compared with the control group (P=0.054), delayed valve closure or leaflet “loitering” during acute posterolateral LV ischemia did not occur.
also conserved with the Tailor ring during acute posterolateral LV ischemia.

Complete ring annuloplasty abolishes leaflet “loitering” and prevents delayed leaflet coaptation in models of acute ovine IMR. The current data suggest that the Tailor ring is equally effective in facilitating timely valve closure and preventing IMR during acute LV ischemia; however, annular reduction with the Tailor ring was also associated with restriction of posterior leaflet motion as found previously with complete rings. We believe that the observed “frozen” posterior mitral leaflet in the setting of mitral annuloplasty is related to reduction of annular area and altered geometric relationships between the posterior mitral annulus and the papillary muscle tips. As the reduction in annular area induced by the Tailor ring is comparable to that achieved with complete rings, this limited posterior leaflet motion may not be surprising. Additionally, “reefing” of the posterior leaflet by the annuloplasty band must also be considered and may be reflected in the baseline differences in posterior leaflet lengths between the 2 groups. Extension of the anterior leaflet during acute IMR has been described in control sheep during acute IMR in a prior report and attributed to papillary muscle “tethering.” In animals with complete annuloplasty rings, systolic anterior leaflet length remained unchanged during acute ischemia, a finding corroborated by the current study. Thus, the Tailor partial flexible annuloplasty ring has essentially the same effects on mitral leaflet motion and geometry during acute LV ischemia in this model as do complete flexible and semi-rigid annuloplasty rings, except that annular flexion is preserved.

Summary

Ring annuloplasty is frequently used in the surgical correction of ischemic mitral regurgitation, and partial flexible ring annuloplasty has been shown to be effective clinically in treating IMR. The current data support this practice as the Tailor partial flexible ring effectively prevented acute IMR in healthy sheep hearts. Surprisingly, as already described under non-ischemic conditions, the Tailor ring altered annular and leaflet in vivo dynamics during ischemia almost identically to that associated with use of complete annuloplasty rings. The Tailor ring prevented mitral annular dilatation, especially in the septal-lateral dimension, facilitated timely valve closure, and converted the mitral valve into a single-leaflet valve by “freezing” the motion of the posterior leaflet. Unlike complete flexible rings, however, the Tailor ring permitted normal annular flexion that was sustained during acute LV ischemia, but the physiologic importance of this annular flexion, if any, in a clinical setting needs further investigation.

Study Limitations

The results of the current study must be interpreted in the context of several limitations. This experimental design does not imitate clinical practice where prior ischemia or infarction is present and then is treated surgically with placement of a ring- in this study, an annuloplasty ring was implanted in a normal heart before the ischemic insult and therefore represented a “prophylactic” surgical correction that is distinctly different than the clinical situation. It is also important to...
emphasize that these findings can only be interpreted in the setting of acute LV ischemia in a normal sheep heart and should not be extrapolated directly to patients with chronic IMR where LV dilatation, sub-valvular geometric perturbations induced by previous infarction and ischemia, and LV remodeling may play a predominant role. This animal model also has other limitations in that sheep have a less well defined posterior annulus than do humans and more atrial tissue above and below the line of leaflet insertion; however, annular dynamics are similar in both humans and sheep.

While the myocardial marker method requires suturing small metal markers to numerous intra-cardiac structures, previous echocardiographic studies show that the markers do not interfere with normal mitral annular or leaflet motion as they are very small (aggregate mass=20±6 mg). Although there were baseline differences in animal size and some hemodynamic parameters between the 2 groups, we believe that these differences did not contribute in an important way to the observed differences in annular and leaflet dynamics between the control sheep and the ring animals.

Acknowledgments

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References

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