Failure of Reduction Annuloplasty for Functional Ischemic Mitral Regurgitation

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Functional ischemic mitral regurgitation (FIMR) is a serious complication of coronary artery disease, and carries a poor prognosis (1-3). Ring annuloplasty combined with coronary artery revascularization is the standard treatment for FIMR. Although the immediate results are excellent, some patients develop recurrent mitral regurgitation (MR) at mid-term follow up. The study aim was to identify possible preoperative echocardiographic parameters that might predict the risk of recurrent FIMR.

Methods: From 124 consecutive patients who underwent revascularization and ring annuloplasty, 48 were selected if they: (i) had a complete preoperative and follow up transthoracic echocardiogram; and (ii) left the operating room with grade 1+ MR. Those patients with moderate or greater late MR were classified as having significant recurrent FIMR (MR group), and those with mild or no MR were classified as no significant FIMR (No-MR group). Left ventricular ejection fraction (LVEF), left ventricular (LV) sphericity, percentage MR jet area, mitral valve tenting area, mitral valve coaptation height, papillary muscle (PM) tethering distance, PM depth, and PM angle were measured by echocardiography preoperatively and at mid-term follow up.

Results: No preoperative differences were found between groups except in posterior PM depth and PM angle. The posterior PM depth and angle in the MR group were significantly smaller than in the No-MR group. In the No-MR group, the posterior PM tethering distance decreased and the PM angle increased significantly with decreasing LV sphericity. In contrast, in the MR group, posterior PM tethering distance, PM depth, and PM angle were unchanged, and the anterior PM depth and PM angle decreased significantly with decreasing LVEF.

Conclusion: FIMR is primarily due to PM displacement, and posterior PM relocation is especially important. Ring annuloplasty does not protect against recurrent FIMR in patients with severe outward displacement of the posterior PM. The severity of posterior PM displacement might be a predictor of ring annuloplasty failure.

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Clinical material and methods

Patients

Between January 1992 and December 2001, 124 consecutive patients with FIMR underwent coronary artery bypass grafting and mitral valve annuloplasty with a flexible Duran ring (Medtronic, Inc.,...
Minneapolis, MN, USA) at the authors’ institution. The presence of FIMR was established intraoperatively with transesophageal echocardiography (TEE), and confirmed visually by the surgeon. In total, 48 patients were selected for the study. The inclusion criteria selected patients who had: (i) complete preoperative and follow up TTE examinations; and (ii) left the operating room with none or grade 1+ FIMR, as evaluated by intraoperative TEE. Patients who had suboptimal echocardiographic windows leading to incomplete anatomic evaluation of FIMR were excluded. The patients were allocated to two groups according to the degree of FIMR at the last follow up TTE examination. Those patients with moderate or greater FIMR were classified as significant recurrent FIMR (MR group), and those with mild or no mitral regurgitation (MR) were classified into the group with no significant recurrent FIMR (No-MR group). Preoperative and last follow up echocardiographic measurements were compared between the two groups.

**Echocardiographic measurements**

Routine TTE examinations, which included two-dimensional (2D) and Doppler echocardiography with color flow mapping, were carried out in all patients, using a standard scanner. All preoperative and last follow up TTE examinations were reviewed by a single operator (A.M.), who measured the following parameters. The severity of FIMR was determined by the ratio of maximum color Doppler regurgitant jet area to left atrial area. MR grade was estimated as mild, moderate, or severe on the basis of ratios of 0-20%, 20-40%, and >40%, respectively (6). LVEF was measured using the modified biplane Simpson method or the single plane area length method (7). LV sphericity (ratio of width to length) was calculated at end-systole in the four-chamber view (8). Systolic mitral leaflet deformation was evaluated by measurement in the mid-systolic apical four-chamber view of the valve ‘tenting area’, delineated by the atrial surface of the leaflets and the plane of the mitral annulus. Valve ‘coaptation height’ was measured as the distance between the leaflet’s coaptation point and the mitral annular plane. The mitral annular diameter was measured in the apical four- and two-chamber views at end-diastole, and the annular area was calculated (9). The displacement of each papillary muscle (PM) was evaluated by calculation of the ‘PM tethering distance’, which was measured as the distance between the PM tips and the contralateral mitral annulus, and the ‘PM depth’, which was the distance between the PM tips and the mitral annular plane in the mid-systolic apical four- and two-chamber views. The ‘PM angle’ was defined as the angle formed by the mitral annular plane and the line connecting the PM tips to the mitral annulus. The anterior and posterior PM angles were calculated as: PM angle = sin⁻¹ (PM depth/PM tethering length). The end-diastolic, mid-systolic, and end-systolic frames were determined as the initial, middle, and last frames of mitral leaflet closure, respectively. All parameters were indexed to the patient’s body surface area (BSA) (Fig. 1).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>MR group (n = 15)</th>
<th>No-MR group (n = 33)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)*</td>
<td>69 ± 10</td>
<td>67 ± 8</td>
<td>NS</td>
</tr>
<tr>
<td>Male/female (n)</td>
<td>7/8</td>
<td>23/10</td>
<td>NS</td>
</tr>
<tr>
<td>NYHA class</td>
<td>2.9 ± 0.7</td>
<td>2.8 ± 0.6</td>
<td>NS</td>
</tr>
<tr>
<td>Ring size (mm)*</td>
<td>27.7 ± 1.0</td>
<td>28.4 ± 1.3</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Follow up period (days)*</td>
<td>931 ± 703</td>
<td>671 ± 744</td>
<td>NS</td>
</tr>
<tr>
<td>Body surface area (m²)*</td>
<td>1.83 ± 0.20</td>
<td>1.94 ± 0.19</td>
<td>0.07</td>
</tr>
</tbody>
</table>

*Values are mean ± SD.
MR: Patients who developed late recurrence of regurgitation; No-MR: Patients without late regurgitation; NS: Not significant.
Statistical analysis

Data were expressed as mean ± SD. To assess inter-group differences, the unpaired Student’s t-test was used for continuous variables, and the chi-square test for categorical variables. The paired Student’s t-test was used to compare intra-group differences. A p-value <0.05 was considered to be statistically significant.

Tenting area, coaptation height, mitral annulus area, PM tethering distance, and PM depth were normalized by BSA to compare the differences between groups.

Results

Patient characteristics

The characteristics of patients undergoing mitral valve annuloplasty combined with coronary artery revascularization are listed in Table I. The MR group comprised 15 patients, and the No-MR group 33. No significant differences were found between the groups in terms of age, gender, preoperative NYHA functional class, duration of follow up, and BSA. However, the ring size in the MR group was significantly smaller than in the No-MR group.

Preoperative echocardiographic measurements

No differences were found between the groups in preoperative percentage MR jet area, mitral annular area, LVEF, LV sphericity, tenting area, coaptation height, anterior and posterior PM tethering distances, anterior PM depth, and anterior PM angle. The only preoperative inter-group differences were a significantly smaller posterior PM depth and PM angle in the MR group (Table II; Figs. 2, 3, and 4).

Follow up echocardiographic measurements

Left ventricular dysfunction and remodeling

At the last follow up TTE, the LVEF in the MR group was significantly lower than in the No-MR group. Although the late LV sphericity had decreased significantly from the preoperative value in the No-MR group, the late LV sphericity in the MR group was still significantly higher than the preoperative value.

Table II: Preoperative and late transthoracic echocardiographic data of patients with late recurrence of regurgitation (MR) and without regurgitation (No-MR).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>MR group (n = 15)</th>
<th>No-MR group (n = 33)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre-op.</td>
<td>Follow up</td>
</tr>
<tr>
<td>Percentage MR jet area</td>
<td>36.7 ± 12.1</td>
<td>25.2 ± 3.9#</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>44.4 ± 9.7</td>
<td>34.7 ± 15.2#</td>
</tr>
<tr>
<td>LV sphericity</td>
<td>0.56 ± 0.07</td>
<td>0.59 ± 0.08#</td>
</tr>
<tr>
<td>Tenting area/BSA (cm²/m²)</td>
<td>0.69 ± 0.33</td>
<td>0.46 ± 0.15#</td>
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<tr>
<td>Coaptation height/BSA (mm/m²)</td>
<td>3.7 ± 1.4</td>
<td>3.0 ± 0.9#</td>
</tr>
<tr>
<td>Mitral annular area (cm²/m²)</td>
<td>10.0 ± 2.2</td>
<td>5.7 ± 0.9</td>
</tr>
<tr>
<td>Anterior PM</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tethering distance/BSA (mm/m²)</td>
<td>20.7 ± 2.0</td>
<td>20.5 ± 2.8</td>
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<tr>
<td>Depth/BSA (mm/m²)</td>
<td>13.8 ± 1.4</td>
<td>12.4 ± 1.5#</td>
</tr>
<tr>
<td>Angle (°)</td>
<td>41.8 ± 4.4</td>
<td>37.7 ± 4.8#</td>
</tr>
<tr>
<td>Posterior PM</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tethering distance/BSA (mm/m²)</td>
<td>21.1 ± 2.8</td>
<td>19.4 ± 2.1</td>
</tr>
<tr>
<td>Depth/BSA (mm/m²)</td>
<td>13.4 ± 2.4*</td>
<td>12.4 ± 2.3#</td>
</tr>
<tr>
<td>Angle (°)</td>
<td>40.5 ± 9.5*</td>
<td>40.7 ± 8.6#</td>
</tr>
</tbody>
</table>

Data are shown as mean ± SD.

*Difference between preoperative TTE in MR group and No-MR group (p <0.05).

#Difference between follow-up TTE in MR group and No-MR group (p <0.05).

BSA: Body surface area; LVEF: Left ventricular ejection fraction; MR: Mitral regurgitation.

p-values are shown for comparison between preoperative condition and follow up in the same group.
group, it had not changed in the MR group. In fact, at follow up, LV sphericity in the MR group was significantly higher than in the No-MR group (Table II; Fig 2).

**Mitral leaflet deformation and severity of mitral regurgitation**

Comparison between the preoperative and last TTE showed that the mitral annular area, tenting area, and percentage MR jet area were significantly reduced from the preoperative values in both groups; this was attributed to the presence of the annuloplasty ring. This reduction, however, was more pronounced in the No-MR group (with the exception of the annular area, which was similar in both groups). Although reduced from preoperative values in both groups, the coaptation height was significantly lower in the No-MR group (Table II).

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**Figure 3: Posterior papillary muscle data.** Preoperative and late echocardiographic measurements in patients with (MR) and without (No-MR) recurrence of regurgitation. BSA: Body surface area; PM: Papillary muscle. *p < 0.05 versus preoperative value.

**Figure 4: Anterior papillary muscle data.** Preoperative and late echocardiographic measurements in patients with (MR) and without (No-MR) recurrence of regurgitation. BSA: Body surface area; PM: Papillary muscle. *p < 0.05 versus preoperative value.
Papillary muscle displacement

In the MR group, the late follow up posterior PM tethering distance, PM depth and PM angle were not significantly different from the preoperative values. In contrast, the posterior PM tethering distance decreased, and the PM angle increased significantly in the No-MR group. The posterior PM depth did not change. At follow up, the posterior PM depth and angle in the MR group were significantly smaller than in the No-MR group (Table II; Fig. 3). Although the anterior PM depth and angle were not different from the preoperative values in the No-MR group, these values were significantly reduced in the MR group. The anterior PM tethering distance did not change in the MR group. At follow up, the anterior PM depth and angle in the MR group were significantly lower than in the No-MR group (Table II; Fig. 4).

Discussion

Mechanism of FIMR

The possible mechanisms responsible for FIMR have been studied extensively, though mostly in experimental animals (10-15). The ischemic insult induces LV geometric changes consisting of heterogeneous mitral annular dilation, increase in sphericity, and outward and apical PM displacement. The results of the present study confirm the data of Otsuji and colleagues (10,16), who showed outward displacement of the PM. This PM displacement increases the distance between the PM tips and the corresponding contralateral portion of the mitral annulus (‘tethering distance’). This distance increase tethers the leaflet down so that it can no longer contact the other leaflet, resulting in regurgitation. The increase in distance is difficult to understand when observing the anatomy of the mitral anterior basal chords. These chords, which arise from each PM, are inserted into the ventricular aspect of the anterior leaflet. Among these basal chords, two particularly thick ‘stay chords’ extend from the PM to the undersurface of the body of the anterior leaflet close to the annulus. In a study of the distribution and direction of the collagen fibers within the anterior mitral leaflet, Cochran et al. (17) have shown that these fibers are oriented from the region of the insertion of the stay chords toward the fibrous trigones. In an acute ovine model, it was found that transection of the two stay chords resulted in an immediate reduction in the aortomitral angle. Functionally, the stay chords hold the apex of the angle, which corresponds to the anterior mitral annulus (18). Also, in a normal porcine model, Lomholt et al. (19) showed that the stay chords sustain three times more tension than their corresponding marginal chords. It is therefore unlikely that the observed increase in tethering distance is due to elongation of the thick stay chords.

The present data show that in FIMR, the PM are displaced outwardly, resulting in the simultaneous elongation of the tethering distance, shortening of the annulopapillary distance (‘PM depth’), and reduction in the angle between the PM tip and the mitral annu-
lus. In fact, the stay chords are the radius of this PM displacement. The stay chords do not allow apical displacement of the PM. It is easy to understand how outward PM displacement reduces its angle with the annulus and brings the PM tips closer to the annulus (‘depth’), but this mechanism does not explain the increase in tethering distance observed in FIMR. It is suggested that this increase in distance is due to the pull of the stay chords on the anterior leaflet: by losing its normal convex curvature, it becomes straighter or even concave, increasing the tethering distance (Fig. 5). Messas and colleagues (20) have shown experimentally that sectioning of the stay chords by freeing the body of the anterior leaflet abolishes its concavity and reduces FIMR.

The results of the present study show that those patients who developed recurrent MR after annuloplasty had smaller anterior and posterior annulopapillary distances (depth) and annulopapillary angles than patients with No-MR. Also, postoperative improvement in FIMR followed the decrease in posterior PM tethering distance and increased posterior PM angle. These findings support previous three-dimensional (3D) echocardiographic studies of ischemic or dilated functional MR that showed outward but not apical PM displacement with reduction of the annulopapillary angle (10,16,21). In a sonomicrometric study of acute FIMR secondary to posterior myocardial infarction, Gorman et al. (12,13) showed that the posterior PM tip moved closer to the annular plane together with a contractile dysfunction of the PM, leading to its elongation.

**Preoperative echocardiographic predictors of ring annuloplasty failure**

Calafiore et al. (5) reported that a preoperative coaptation height of 11 mm or more was a predictor of residual MR in patients with ischemic or idiopathic cardiomyopathy who underwent mitral valve annuloplasty. In the present study, no patient had a coaptation height ≥ 11mm, and no difference in preoperative coaptation height between those with or without recurrent mitral regurgitation was found. The patients studied by Calafiore et al. had more severe dilated cardiomyopathy than did the present cohort. In the former series, the mean preoperative LVEF was 27% and the LV sphericity index 0.81. In the present patients, the LVEF was 40% and the LV sphericity index 0.58. Although the more severe the sphericity the higher the risk of recurrence of FIMR, both groups of the present patients had similar preoperative LVEF and LV sphericity. A search for risk factors of FIMR recurrence in patients with less evolved LV dysfunction seemed appropriate.

In the present study, no preoperative differences between those patients with late MR and No-MR in terms of mitral valve deformation (tenting area and coaptation height) and left ventricular function (LVEF) and distortion (sphericity) were found. The only difference was the smaller depth and angle of the posterior PM in the group of patients with recurrent MR versus those with no late MR. These findings suggest that in those patients with severe outward displacement of the posterior PM, a simple ring annuloplasty does not protect against the recurrence of MR. Clearly, these findings are an index of the preoperative severity of PM displacement. The fact that all patients (including those who developed recurrent MR) left the operating room with no or grade 1+ regurgitation points toward a progression in LV remodeling. It can be hypothesized that although severe annulus reduction induces immediate valve competence, beyond a certain degree of PM displacement, the tension on the subvalvular apparatus is such that further PM displacement occurs. The easy echocardiographic measurement of posterior PM displacement appears to be a useful method to determine the likelihood of success or failure of ring annuloplasty in patients with moderately depressed LV function. In these patients, it can be argued that more severe ring undersizing might ensure long-lasting leaflet coaptation. This is unlikely because the ring size in the MR group was significantly smaller than in the No-MR group (27.7 versus 28.4). Also, the indexed coaptation height (as an indicator of apical displacement of the leaflets) was significantly higher in the MR group. If anything, the MR group had a more immediate successful annuloplasty. However, the preoperative degree of posterior papillary lateral displacement might be used to determine the ring size.

**Study limitations**

The present study used a retrospective analysis of routine clinical echocardiographic data. Estimation of geometric changes in the mitral valve apparatus was carried out using 2D echocardiography; therefore, 3D PM displacement could not be evaluated (as with 3D echocardiography). However, previous reports support the adequacy of 2D echocardiography for measuring PM displacement (22-24).

Herein, the mechanism of recurrent MR in patients with FIMR who underwent mitral valve annuloplasty combined with revascularization was investigated, but the grade of MR was evaluated only semi-quantitatively, and LVEF in some patients was not calculated using the modified biplane Simpson method.

Finally, in the present study, the number of patients was relatively small, and the mean BSA of the MR group was slightly less than that of the No-MR group (p = 0.07). This may have been the reason for differences in ring size between the groups. Further investi-
gations might address these issues prospectively.

In conclusion, FIMR is primarily due to PM displacement, and posterior PM relocation is especially important. In those patients with severe outward displacement of the posterior PM, reduction annuloplasty does not protect against recurrent FIMR, which is secondary to left ventricular dysfunction and dilation and bilateral PM displacement. The severity of posterior PM displacement might be a predictor of ring annuloplasty failure in patients with FIMR.

References
18. Goetz WA, Lim HS, Lansac E, et al. The aortomitral angle is suspended by the anterior mitral basal “stay” chords. Thorac Cardiovasc Surg 2003;51:190-195
23. Otsuji Y, Kumanohosato T, Yoshihuku S, et al. Isolated annular dilation does not usually cause important functional mitral regurgitation. J Am...
Meeting discussion

DR. JEAN-G. DUMESNIL (Sainte-Foy, Quebec, Canada): Were the patient groups similar with regard to taking ACE inhibitors and beta-blockers? Because this implies left ventricular remodeling, it would be important to know if they were all taking ACE inhibitors.

DR. STEPHEN A. TAHTA (Missoula, MT, USA): In general, the patients were managed in the same way - at least in the early postoperative period. I would think that there was no difference.

DR. DUMESNIL: I think this has important clinical implications. You said that there were no ischemic events, so obviously it’s remodeling - which could possibly be prevented by ACE inhibitors and/or beta-blockers in these patients as, initially, they had low ejection fractions.

DR. TAHTA: Based on our aggressive surgical program, the patients were treated the same postoperatively, with beta-blockers and ACE inhibitors. I cannot say whether there were any changes in medical treatment for the longer term follow up.

DR. DUMESNIL: It might be interesting to look at that point.

DR. KARYN KUNZELMAN (Madison, WI, USA): Were you able to measure the distance between the two papillary muscle tips in terms of whether they are moving apart, or not? Also, do you have any thoughts on trying to bring the papillary muscle tips back closer together to address ischemic MR, in addition to the ring?

DR. TAHTA: I cannot provide any data on measurements between the papillary muscles. But some groups are looking at that distance and clearly it is increased. I would assume that the distance is increased, but we looked at left ventricular sphericity, which was increased in patients with recurrent MR, though the change was not statistically significant. Techniques to reapproximate the papillary muscles make a lot of sense. Based on our data, I would postulate that by trying to reapproximate the papillary muscles, you are probably changing the papillary muscle angle that we described, trying to return it to a more normal angle. That may be one explanation for why there is better success at preventing recurrent MR.

DR. PRAVIN M. SHAH (Newport Beach, CA, USA): You say that the decrease in depth was a surprise, but I would have expected the opposite. You explained it on the basis of lack of chordal elongation, but did you measure the tenting area, tethering area, the annulus around the area, to support that hypothesis that the cords were indeed shorter in one group compared to the other?

DR. TAHTA: We measured the tethering area, and there was no statistical difference, but that may have been due to the small number of patients.

DR. CHRISTOPHE ACAR (Paris, France): I was slightly confused by your presentation. Until now, I thought that the tenting area was a parameter which would allow measurement of the restriction. So the larger the area, the more the restriction. But you show that the tenting area decreases in patients with recurrent MR. I don’t understand the mechanics of this.

DR. TAHTA: It is slightly confusing, but it may been related to the fact that the papillary muscle depth was shortened rather than lengthened. I think that is surprising, because most of the theory which would support what you’re saying involves displacement of the papillary muscle towards the apex as opposed to towards the base. It’s likely that our patient numbers were too small to make any conclusions with respect to the tenting area.

DR. ACAR: Do you think that, technically, the tenting area is as easy to measure after ring annuloplasty as it is before? Having a prosthetic ring in place may make measurement more difficult.

DR. TAHTA: Yes, that’s a good point - it is probably true.

DR. SHAH: Another aspect is that for the interpapillary muscle distance, the short-axis views might be the best way of measuring it, because in one particular view you can see both papillary muscles and that might be good enough. Another point is that in many transventricular studies we use a routine approach, but to assess this type of measurements you probably need techniques that are a little off axis to maximize the information.

DR. D. CRAIG MILLER (Stanford, CA, USA): Dr. Tahta, you’ve asked us to turn our world upside down, basically. I’m also confused - perhaps because this is the first study after ring annuloplasty to look at mechanisms. Is that why things appear to be different?

DR. TAHTA: That could be part of the problem. I agree that it is much more difficult to look at the tenting area when the ring is in place.

DR. MILLER: But you calculated a tenting distance - and surprisingly, it went down in those patients who later had a paravalvular leak - which none of us would have expected. Perhaps we are confused because this is a brand new approach, and you should pursue it.
What would have happened with a rigid complete ring?

**DR. TAHTA**:
Perhaps putting in a small ring would have an effect, because we certainly changed significantly, at least the annulus, whether it’s a flexible or a rigid ring. We’re significantly decreasing the annular diameter and that might have some effect.

**DR. SHAH**:
Are these all rings, or some of them are bands?

**DR. TAHTA**:
They are all flexible rings.

**DR. CARLOS DURAN** (Missoula, MT, USA):
We must not forget what the aim of the study was. We were not seeking the new geometry after ischemic mitral regurgitation, or the mechanism of ischemic mitral regurgitation. The aim was whether any parameter would indicate that in a particular patient the ring would not solve the problem. All we are saying is that the bigger the displacement, the less the chance of success. There may be other parameters that are easier to measure and would tell us the same thing - the severity of papillary muscle displacement. We began with sphericity, but found that the shorter the distance between the papillary muscle and the annulus, the less likelihood of success. Whether that would change if you used a different type of ring, we don’t know.

**DR. SHAH**:
That fits, but neither the tenting area nor the depth fit. As Dr. Miller pointed out, this study may be the first to examine the point, and perhaps we have to rethink the situation. However, some aspects do fit - the angle is absolutely correct, because the decrease in angle suggests more lateral displacement.

**DR. DURAN**:
So the more you decrease the angle, the less the distance between the tip of the papillary muscle and the annulus.

**DR. SHAH**:
I understand.

**DR. WILLIAM NORTHRUP** (Minneapolis, MN, USA):
Can we surmise that recommendations with regard to refinements in the surgical treatment of ischemic MR will involve chordal cutting both from the anterior and the posterior leaflet? Is this a future suggestion based on some of these data?

**DR. TAHTA**:
I have recently spoken to Dr. David, who surmised that cutting the stay cords may be the best way to reduce or prevent recurrent MR. That has been very successful, and MR has not recurred in 20 patients over a one-year period. But it’s not necessarily the solution - there may be no recurrent MR because the follow up time is too short. Other groups are trying to reapproximate the papillary muscles and, with an annuloplasty ring, trying to reconstruct normal anatomy. That’s a better way to go, and it will probably have a better long-term success.