

# Midterm results of edge-to-edge mitral valve repair without annuloplasty

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**Objective:** Edge-to-edge mitral valve repair is usually performed in association with annuloplasty, with rare exceptions. We retrospectively analyzed the results of ringless edge-to-edge repair, particularly in view of minimally invasive and percutaneous approaches.

**Methods:** From November 1993 to December 2001, 81 patients underwent edge-to-edge mitral repair without associated annuloplasty. The cause was degenerative in most patients. In 32 patients the annulus was severely calcified. Type I lesions were present in 6 patients, type II lesions in 60 patients, and type III lesions in 15 patients. A double-orifice repair was done in 69 patients, and paracommissural repair was done in 12 patients. In 5 patients edge-to-edge repair was used as a rescue procedure.

**Results:** There were 3 hospital and 4 late deaths, for a 4-year survival of  $85\% \pm 6.7\%$ . At latest follow-up, 63 patients were in New York Heart Association classes I or II, and 9 patients were in classes III or IV. Nine patients required reoperation ( $89\% \pm 3.9\%$  overall freedom from reoperation at 4 years). Annular calcification was associated with a greater reoperation rate ( $77\% \pm 22\%$  vs  $95\% \pm 4.6\%$  freedom from reoperation,  $P = .03$ ). Intraoperative water testing and postrepair transesophageal echocardiography predicted late failure. Only 1 of 42 patients required reoperation in the follow-up period when annular calcification, rheumatic disease, or rescue procedure were not present as risk factors.

**Conclusions:** Our data confirm overall suboptimal results of the edge-to-edge technique when annuloplasty is not added to the repair. Annular calcification, rheumatic cause, and edge-to-edge repair done as a rescue procedure were associated with the worst outcome. Midterm results in selected patients encourage future developments in catheter-based edge-to-edge procedures.

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Read at the Eighty-third Annual Meeting of The American Association for Thoracic Surgery, Boston, Mass, May 4-7, 2003.

Received for publication April 30, 2003; revisions requested June 6, 2003; revisions received June 22, 2003; accepted for publication July 10, 2003.

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J Thorac Cardiovasc Surg 2003;126:1987-97

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0022-5223/2003 \$30.00 + 0

doi:10.1016/S0022-5223(03)01291-1

**A**nnuloplasty is commonly recommended to complete mitral valve repair operations because its use has been associated with improved long-term durability.<sup>1,2</sup> However, some groups have debated the need for annuloplasty on a routine basis for every valve repair procedure. There are recent reports of comparable durability without annuloplasty in selected groups of patients. In these series, however, some sort of annular support was obtained by using either continuous<sup>3</sup> or interrupted<sup>4</sup> annular sutures. Annuloplasty is not considered mandatory in cases involving a small preoperative mitral annulus (eg, acute mitral regurgitation [MR]).

Redefining the exact role for annuloplasty in mitral valve repair procedures is urged by recent developments of minimally invasive approaches and beating-heart

**TABLE 1. Preoperative clinical and echocardiographic data**

Preoperative clinical data	N	%
Sex		
Female	37	46%
Male	44	54%
Functional class		
NYHA I	4	5%
NYHA II	29	36%
NYHA III	44	54%
NYHA IV	4	5%
Preoperative rhythm		
Sinus rhythm	64	79%
Atrial Fibrillation	16	20%
Pacemaker*	4	5%

Preoperative Doppler echocardiographic data	Mean ± SD	Range
Ejection fraction	56.7% ± 9.9%	20%-80%
LVEDD (mm)	63.9 ± 11.4 mm	51-93
LVESD (mm)	42.6 ± 12.7 mm	24-70
Left atrial diameter (mm)	48.4 ± 9.1 mm	38-70
PAPs (mm Hg)	44.6 ± 20.3	17-110†
Mean preoperative MR grade	3.78 ± 0.47	2/4-4/4‡

*LVEDD*, Left ventricular end-diastolic diameter; *LVESD*, left ventricular end-systolic diameter; *PAPs*, systolic pulmonary artery pressure.

\*Three of the patients with pacemakers are in another category also.

†Thirty patients had pulmonary hypertension, which was defined as a systolic pulmonary artery pressure of greater than 30 mm Hg.

‡Sixty-five patients had 4/4 MR (80.2%), 14 patients had 3/4 MR (17.3%), and 2 patients with SAM in hypertrophic obstructive cardiomyopathy had 2/4 MR (2.5%)

solutions for correction of MR. A recent report<sup>5</sup> introduced the concept of feasibility of closed-heart procedures for the treatment of mitral valve regurgitation by applying a ringless edge-to-edge technique<sup>6</sup> methodology with dedicated instruments.

Herein we report a retrospective analysis on our clinical experience with the edge-to-edge technique without annuloplasty.

## Methods

From November 1993 through December 2001, of 442 patients with mitral valve regurgitation treated with the edge-to-edge technique, 92 (20.8%) underwent the procedure without the association of any sort of annuloplasty (patients who had a suture annuloplasty, either complete or segmental, were excluded as well). Eleven additional patients who had the repair done with the minimally invasive approach were also excluded to avoid the influence of the learning curve of those specific surgical techniques. The following analysis refers to the remaining group of 81 patients. There were 37 (46%) female and 44 (54%) male patients, with a mean age of 64.9 ± 12.6 years. Preoperative clinical data are reported in Table 1. At admission, 33 (41%) patients were in New York Heart Association (NYHA) class I or II, whereas 48 (59%) patients were in class III or IV. The majority of patients (79%)

**TABLE 2. Cause of the MR**

Cause	N	%
Degenerative	57	70
Myxomatous, n = 35		
Fibroelastic, n = 22		
Functional	12	14
Ischemic, n = 10		
DCM, n = 2		
Rheumatic	6	7.5
Endocarditis	4	5
Inactive, n = 3		
Active, n = 1		
SAM in HOCM	2	2.5

*DCM*, Dilated cardiomyopathy; *SAM*, systolic anterior motion; *HOCM*, hypertrophic obstructive cardiomyopathy.

were in sinus rhythm. Nine (11%) patients had a left ventricular ejection fraction of less than 45%.

Transesophageal echocardiography (TEE) was performed the day before the operation in most patients. MR was severe in most patients, with a mean degree of 3.78 ± 0.47. The cause of MR is reported in Table 2, showing the prevalence of degenerative disease (70%). The main mechanism of regurgitation included Carpentier classification<sup>2</sup> type 1 lesions in 6 patients, type 2 lesions in 60 patients, and type 3 lesions in 15 patients. In 22 patients a single segmental lesion was identified at preoperative Doppler echocardiographic examination and confirmed at surgical inspection, whereas in the remaining 57 (70%) patients, more than one segmental lesion was demonstrable. In 2 patients with hypertrophic obstructive cardiomyopathy, no mitral lesions were present (they were classified as type 1 lesions), and the edge-to-edge technique was used to correct the systolic anterior motion of the anterior leaflet associated with left ventricular outflow tract obstruction and moderate MR. A comprehensive list of the anatomic findings is reported in Table 3.

Severe annular calcification was found in 32 patients. In 19 patients the posterior annulus was completely calcified, mostly with extension of the calcific lesion into the lateral free wall of the left ventricle, whereas in the remaining 13 patients annular calcification was segmental, nevertheless preventing quadrangular resection or prosthetic ring implantation.

Associated cardiac conditions included coronary artery disease in 20 patients, aortic valve disease in 6 patients, left ventricular aneurysm in 4 patients, ascending aortic aneurysm in 3 patients, chronic aortic dissection in 1 patient, dilated cardiomyopathy in 3 patients, and hypertrophic obstructive cardiomyopathy in 2 patients; 1 patient had previous coronary artery bypass surgery.

## Surgical Procedure

The surgical technique has been described in detail in previous reports.<sup>7,8</sup> The surgical approach to the mitral valve was through a standard left atrial incision in 76 patients. In 4 patients mitral repair was carried out through the left ventricular opening during aneurysm resection, and in 1 patient it was carried out through the aortic valve during a Bentall procedure. Valve inspection and segmental analysis was carried out in a standard fashion, and the edge-to-edge technique was selected only in those cases in which

more conventional repair techniques were considered not suitable or carried a high risk of unsatisfactory results.

A double-orifice repair was performed in 69 (85%) patients: this was an isolated, central edge-to-edge suture in 67 patients, and in 2 patients the central suture was associated with commissural edge-to-edge repair (1 in the posterior and 1 in the anterior commissure). In the remaining 12 patients with a paracommissural repair, it was posteriorly located in 9 patients and anteriorly located in 3 patients. A 4-0 polypropylene continuous suture without pledgets was used in most cases for leaflet approximation unless the leaflets were very thin. In these cases a 5-0 suture was preferred; pledgets were rarely used to reinforce the repair.

In case of annular calcification, the rationale for adopting the edge-to-edge technique was to correct leaflet lesions with no annular manipulation.

In 10 patients, in combination with the edge-to-edge technique, an associated repair procedure was carried out, including quadrangular resection (5 patients), subcommissure obliteration (3 patients), neochordae implantation (1 patient), and triangular resection of the anterior leaflet (1 patient).

The edge-to-edge technique was used as a rescue procedure in 5 patients: a double-orifice repair was done after quadrangular resection (2 patients), neochordae implantation (1 patient), and simple annuloplasty (1 patient). In 1 patient anterior paracommissural edge-to-edge repair was used to correct commissural leakage after quadrangular resection of the posterior leaflet. In 3 patients a previously implanted ring was removed after the edge-to-edge repair to prevent valve stenosis.

Valve competence was assessed in all patients with forced saline injection in the left ventricle during cardioplegic arrest, excluding those patients having the repair carried out through the ventricle or the aortotomy. Water-testing data were therefore available in 76 (94%) patients. After discontinuation of cardiopulmonary bypass, valve function and anatomy were assessed by means of intraoperative TEE (data available on 74 patients).

A number of associated procedures were carried out concomitantly with valve repair, including coronary artery revascularization (16 patients), aortic valve replacement (5 patients), left ventricular aneurysmectomy (4 patients), radiofrequency ablation of atrial fibrillation (3 patients), ascending aorta replacement (2 patients), myotomy-myectomy (2 patients), the Bentall procedure (1 patient), and patent foramen ovalis closure (1 patient).

### Data Collection and Statistical Analysis

Intrahospital data were collected through a hospital database and controlled on patients' records. Follow-up data were obtained by means of outpatient visit, including a TEE examination, or by means of telephone interview with the patients and the referring cardiologists, collecting, when available, the latest Doppler echocardiographic findings. Follow-up information was obtained during the month of February 2003. All patients had at least 1 year of follow-up at that time. Follow-up was completed in 79 (97.5%) patients, with Doppler echocardiographic data available for 76 patients. Mean follow-up time was  $2.9 \pm 1.8$  years (230 patient-years).

For patients who underwent reoperation during the follow-up period, clinical and Doppler echocardiographic data refer to the latest findings available before reoperation.

**TABLE 3. Segmental analysis at 2-dimensional echocardiography and surgical inspection**

	Type I*	Type II	Type III	Total
Anterior leaflet lesions				
A1	1	12	0	13
A2	2	41	2	45
A3	0	14	1	15
Posterior leaflet lesions				
P1	1	15	8	24
P2	0	48	12	60
P3	0	24	10	34

\*Two patients with systolic anterior motion, classified as type I predominant lesions, are not included in this table because no valve-motion alterations were recognized by means of echocardiography or at surgical inspection other than the systolic anterior motion of the anterior leaflet caused by hypertrophic cardiomyopathy.

The variables analyzed as risk factors for reoperation are reported in Table 4. Data were analyzed with the Statistical packages JMP for Mac and SAS 8.2 for Windows (SAS Institute). For continuous variables, differences were tested with the unpaired *t* test, whereas for categorical variables, the  $\chi^2$  method was used. Linear regression analysis was performed for correlation between continuous variables.

Freedom from events (death and reoperation) was analyzed with actuarial methods. Results are reported at 4 years because after this limit, the number of patients at risk was too small. Differences on actuarial life tables were analyzed by using the log-rank method.

Univariate and multivariate analysis of risk factors was performed with Cox proportional hazards regression. The Wald test was used to compute the significance of risk. The variables showing either statistical significance or a hazard ratio of greater than 3 were inserted into a multivariable model.

## Results

### Hospital Mortality and Long-Term Survival

Three patients died within 30 days of the operation, for a hospital mortality of 3.7%. Causes of hospital deaths included low cardiac output syndrome and multiorgan failure in 2 patients with preoperative left ventricular dysfunction, whereas one patient died of hemoperitoneum and hemorrhagic shock. There were 4 late deaths, for a 4-year survival of  $85.9\% \pm 6.7\%$ . The cause of late death was unknown in 2 patients, sudden in 1 patient, and related to pulmonary infection and septic shock in 1 patient with preoperative chronic pulmonary hypertension. Excluding the latter patient, who had moderate MR at the latest follow-up, MR was less than moderate in all patients who died during the follow-up period.

### Reoperation

Nine patients required reoperation during the follow-up period. The cause of reoperation was recurrent severe regurgitation in all cases. Mitral valve replacement was done

**TABLE 4. Analysis of risk factors for reoperation**

Univariate predictor variable	Hazard ratio from proportional hazards regression	P value from proportional hazards regression	P value from multivariable analysis
Age at operation	0.9928	.7351	—
Preoperative NYHA class	0.9453	.9086	—
Preoperative ejection fraction	1.071	.1107	—
Preoperative LVESD	0.9303	.3382	—
Preoperative LVEDD	0.9714	.62	—
Pulmonary hypertension at rest	1.6342	.5773	—
Nonsinus heart rhythm	1.1584	.8547	—
Cause (degenerative)	0.7796	.7567	—
Cause (functional)	0	.9952	—
Cause (rheumatic)	<b>3.5993</b>	<b>.1105</b>	—
Cause (endocarditis)	0	.9955	—
Cause (other)	0	.9954	—
Main mechanism of MR (type I, II, or III*)	1.3114	.6723	—
A1 disease	0.5239	.5429	—
A2 disease	1.5402	.5432	—
A3 disease	0.4389	.4377	—
P1 disease	0.7297	.672	—
P2 disease	2.1805	.4658	—
P3 disease	0.6023	.4791	—
Presence of more than one lesion	0.651	.5469	—
<b>Annular calcification</b>	<b>4.1833</b>	<b>.047</b>	—
Approach other than left atriotomy	0	.993	—
Central versus commissural edge-to-edge	0	.9948	—
Associated repair manoeuvres	1.3759	.6913	—
<b>Edge-to-edge procedure done as rescue</b>	<b>8.7301</b>	<b>.0141</b>	<b>.04</b>
Small annulus as contraindication	1.6766	.475	—
<b>Leak at water testing</b>	<b>5.7199</b>	<b>.0142</b>	<b>.02</b>
<b>MR at intraoperative TEE</b>	<b>3.2052</b>	<b>.0831</b>	—
<b>MR at predischarge Doppler echocardiography</b>	<b>2.0194</b>	<b>.0483</b>	—

In bold are the variables with a *P* value lower than .05 or with a hazard ratio greater than 3.

LVEDD, left ventricular end-diastolic diameter; LVESD, left ventricular end-systolic diameter.

\*According to Carpentier classification.

in all reoperations, and in all but 2 patients, a mechanical prosthesis was used. Overall freedom from reoperation was  $89\% \pm 3.9\%$  at 4 years. Figure 1 depicts actuarial freedom from reoperation according to the early result of valve repair. More than trivial residual MR at intraoperative post-repair Doppler echocardiography (Figure 1, *a*) was associated with lower freedom from reoperation at 4 years ( $67\% \pm 32.7\%$  vs  $94\% \pm 5.8\%$ ,  $P = .03$ ). Suboptimal water-testing results (Figure 1, *b*) were associated with lower freedom from reoperation ( $61\% \pm 38.9\%$  vs  $98\% \pm 1.8\%$ ,  $P = .005$ ). Figure 2 shows that freedom from reoperation at 4 years was lower in patients with annular calcification than in those without it ( $77\% \pm 22\%$  vs  $95\% \pm 4.6\%$ ,  $P = .03$ ). No patients with paracommissural repair required reoperation during the follow-up period. Table 4 lists the hazards ratios derived from proportional hazard regression analysis for all perioperative variables. The 6 variables (rheumatic cause, annular calcification, edge-to-edge technique used as a rescue procedure, water-testing leak, MR at intraoperative TEE, and MR at predischarge Doppler echocardiography) showing either statistical significance or a hazard ratio of greater than 3 were inserted into a multivariable model; in the 6-variable model no variable showed statistical significance because of the high correlation of the variables. Stepwise variable selection methods on this model created a 2-variable model, identifying water-testing leak ( $P = .02$ ) and rescue ( $P = .04$ ) as the important variables.

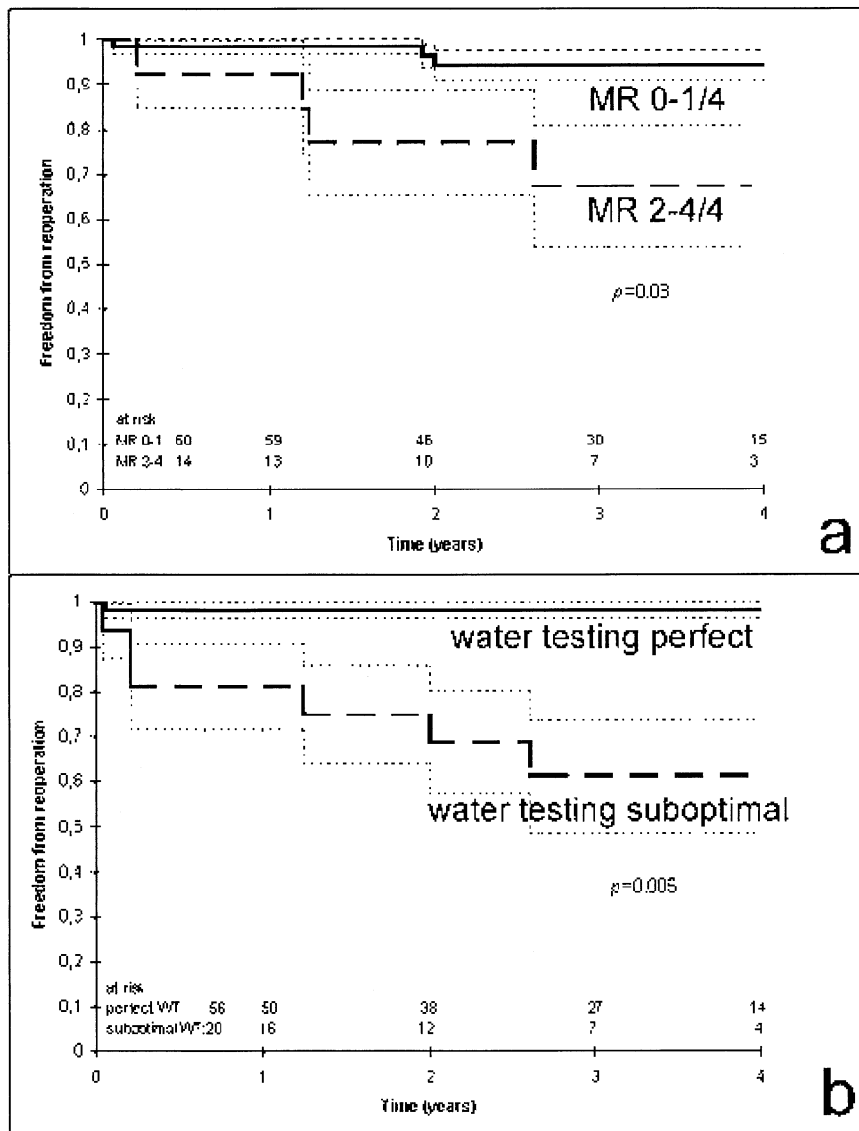
Excluding patients with annular calcification, rheumatic disease, and edge-to-edge repair as a rescue procedure, only 1 of 42 patients needed reoperation in the follow-up period compared with 8 of 37 patients with these risk factors ( $P = .005$ ).

### Evaluation of the Repair

**Water testing.** Among the 76 patients whose water-testing results were available, some degree of mitral valve leaking at intraoperative water testing was detected in 19 patients: in 13 patients it was mild, whereas in 6 patients it was graded as moderate but judged acceptable for that particular anatomic and clinical context. The reoperation rate was higher in those patients having an abnormal water-testing result (with any degree of leakage) versus in those who showed good competence of the valve ( $37\%$  vs  $7\%$ ,  $P = .003$ ).

Patients with abnormal intraoperative water-testing results had a higher risk of late mortality. The mean water-testing grade (see below) was  $1.0 \pm 0.24$  in patients who died during follow-up versus  $0.2 \pm 0.07$  in those who survived ( $P = .006$ ).

**Postrepair Doppler echocardiographic assessment.** Mitral incompetence at intraoperative TEE (data available on 74 patients) and after weaning from cardiopulmonary bypass was absent or trivial (0/4 or 1/4) in 60 patients, whereas



**Figure 1. a, Freedom from reoperation according to intraoperative postrepair MR Doppler echocardiographic grade (MR grade 0-1 vs MR grade 2-4). b, Freedom from reoperation according to intraoperative water testing (perfect vs suboptimal).**

it was 2/4 in 11 patients and 3/4 in 3 patients (2 elderly patients with ischemic MR and severely decreased left ventricular function and 1 patient with degenerative MR and a severely calcified annulus). One of these 3 patients died in the early postoperative period, and the 2 survivors were still alive at the time of follow-up, with stable 3/4-grade MR (they were in NYHA functional classes I and II, respectively). Preoperative pulmonary hypertension ( $P = .02$ ), cause (higher incidence in rheumatic patients,  $P = .001$ ), and annular calcification ( $P = .05$ ) were risk factors at univariable analysis for immediate postrepair residual MR of grade 2 or higher, but none of these variables were

statistically significant risk factors for reoperation at multivariable analysis.

The degree of water-testing leakage was linearly correlated to TEE MR grading ( $r^2 = 0.589$ ,  $P < .0001$ ). Abnormal water-testing results predicted a postoperative MR grade of greater than 1/4 with 93% sensitivity, 89% specificity, 65% positive predictive value, and 98% negative predictive value.

Transthoracic Doppler echocardiography was repeated before discharge in 73 patients and showed a higher prevalence of MR grade 2/4 and higher compared with that at intraoperative examination. Pre-discharge Doppler MR

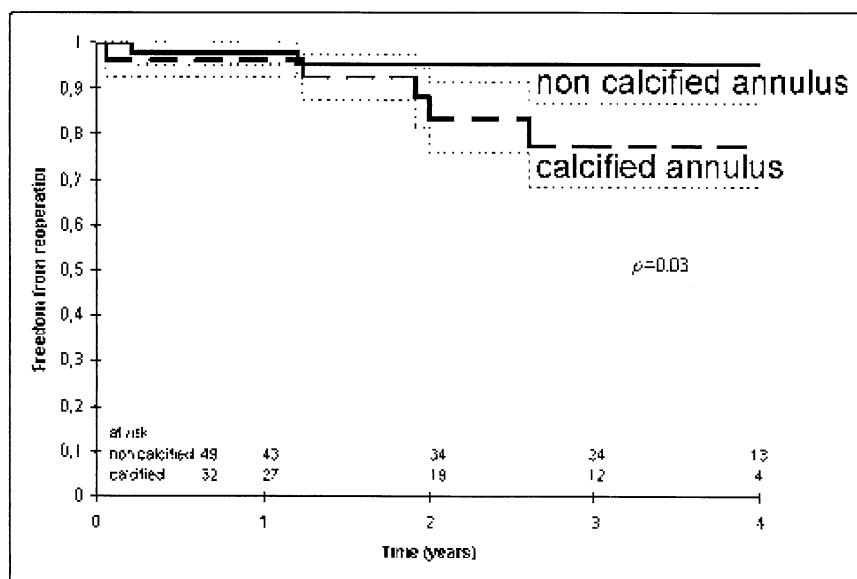


Figure 2. Freedom from reoperation according to the presence of annular calcification.

grade of greater than 1/4 did correlate with need for reoperation, although not statistically significantly ( $P = .06$ , Table 5). The degree of mitral incompetence at last follow-up, including those patients who required reoperation, is shown in Table 5. The mean MR grade was  $2.1 \pm 1.4$  in the group of patients with rheumatic cause, annular calcification, or the edge-to-edge technique done as a rescue procedure compared with  $1.4 \pm 1.02$  in the remaining population ( $P = .008$ ).

Mitral stenosis was detected in no patients either during the hospital stay or during follow-up.

### Clinical Status

At the latest follow-up, 41 patients were in NYHA class I, 22 in class II, and 9 in classes III and IV. NYHA class and residual MR at latest follow-up were linearly correlated ( $r^2 = 0.20$ ,  $P < .0001$ ).

Data on heart rhythm at follow-up were available in 70 patients, with 51 being in sinus rhythm (including one with a pacemaker implanted) and 19 in atrial fibrillation. Patients in atrial fibrillation had more severe symptoms: the mean NYHA class in the sinus rhythm group was  $1.4 \pm 0.09$  versus  $1.9 \pm 0.68$  in the atrial fibrillation group ( $P = .01$ ). Patients without annular calcification, rheumatic disease, and edge-to-edge repair done as a rescue procedure tended to have less symptoms (one in class III and one in class IV at latest follow-up,  $P = .01$ ).

During the follow-up period, 29 patients required rehospitalization (including those who underwent reoperation). Freedom from rehospitalization was  $56\% \pm 43\%$  at 4 years. The rehospitalization rate was higher in those patients with suboptimal reconstruction: freedom from rehospitalization

at 4 years was  $67\% \pm 33\%$  in those patients with normal competence at intraoperative water testing, whereas it was  $56\% \pm 43\%$  in those who had some degree of leak at intraoperative testing ( $P = .01$ ). The most common cause of hospitalization was supraventricular arrhythmia (14 patients), followed by congestive heart failure (9 patients), acute endocarditis (1 patient), and acute myocardial infarction (1 patient). Hospitalization was not related to heart disease in 4 patients.

Two patients had minor cerebrovascular accidents in the follow-up period.

### Discussion

Retrospective analysis of our data confirmed that when annuloplasty is not performed in combination with the edge-to-edge procedure, midterm results are suboptimal when compared with those of edge-to-edge repair associated with annuloplasty.<sup>7</sup> During the follow-up period, the number of patients with significant MR (greater than 1/4 grade) increases compared with discharge findings, suggesting a propensity toward progression of the disease. Similar findings have been reported by Flameng and colleagues<sup>9</sup> in a group of 242 patients with degenerative MR submitted to valve repair and followed up with serial Doppler echocardiographic examinations over a period of 8 years. The authors found that the durability of successful mitral valve repair is not constant, with some subgroups of patients having severe regurgitation late in the follow-up period. The linearized rate of recurrence of severe ( $>2/4$  MR grade) regurgitation was 3.7% per year, and it was higher when annuloplasty ring implantation was not added to the repair

**TABLE 5. Early and late evaluation of the repair**

Intraoperative: water testing by means of saline injection (0-2)*						
	0	1	2		Total	P
N (reoperated)	56 (3)	14 (6)	6 (0)		76	.001
Postoperative: Doppler echocardiography (0-4)						
	0, 1/4	2/4	3/4	4/4	Total	P
After CPB	60 (5)	11 (4)	3 (0)	0	74	.06
Before discharge	55 (5)	15 (3)	3 (1)	0	73	.20
Latest follow-up	35	24	9 (2)	8 (7)	76	

In parentheses is the number of reoperated patients for each subgroup. Statistical significance refers to the probability of undergoing reoperation on the basis of each assessment of valve competence.

\*0, Water testing normal; 1, mild leak; 2, evident leak. Water testing was not performed in 5 patients who had a transventricular or transaortic approach.

procedure. Progression of MR might partially be related to an inadequate surgical technique, but it could also be caused by intrinsic tissue degeneration. In our series we found similar results when Doppler echocardiographic findings were analyzed in detail at the latest follow-up. However, because patients were not prospectively followed up with serial Doppler echocardiographic examinations, timetable analysis of the recurrence of MR was not feasible, and inferences could only be driven by reoperation rate analysis.

The benefits of annuloplasty in valve repair have been reported by several authors, although the indication on a routine basis has been occasionally questioned. Gillinov and associates,<sup>1</sup> in a large review of the Cleveland Clinic valve repair experience on more than 1000 patients, found that leaflet resection without annuloplasty was a risk factor for late failure. These data are supported by the general opinion that mitral annuloplasty not only remodels the annulus to force leaflet coaptation but also stabilizes the repair over time, reducing the risk of late failure. Computational models have also predicted lower stresses applied on the leaflets when annuloplasty is associated with the repair,<sup>10</sup> reducing the risk of progressive degeneration or rupture of the reconstruction.

However, implantation of an annuloplasty prosthesis is associated with a number of drawbacks and potential hazards, including reduction of annular 3-dimensional motion, immobilization of the posterior leaflet, prolongation of ischemic time, dehiscence, infection, hemolysis, lesions to structures (atrioventricular node, aortic valve, circumflex artery, and mitral leaflets), atrioventricular groove rupture, asymmetric implantation, and valve distortion. To avoid these risks, some authors suggest a more selective use of annuloplasty prostheses, reporting excellent results with ringless mitral repair for both posterior and anterior leaflet lesions.<sup>4,11</sup>

### Study Population and Bias of Selection

Higher failure rates for the edge-to-edge technique without ring annuloplasty were anticipated on the basis of a recent analysis of a group of 260 patients submitted to the double-

orifice technique, in which those who received an annuloplasty had a  $92\% \pm 3.4\%$  freedom from reoperation at 5 years compared with a  $70\% \pm 15.0\%$  freedom from reoperation in those who had a ringless repair ( $P = .02$ ).<sup>7</sup> Reasons to avoid ring annuloplasty in the present study included annular calcification, approaches other than left atriotomy, small preoperative valve area carrying higher risk of postrepair stenotic valve, and risk of systolic anterior motion. In some cases the decision was biased by the attempt to reduce the ischemic time during complex operations, either because of left ventricular dysfunction or because of associated procedures. For these reasons, the present study population markedly differed from those of our previous reports: associated procedures were more than double, clinical status was more compromised, and left ventricular function was more decreased than in the previously reported series.<sup>6-8</sup>

As a result of this case mix, both early and late mortality in this series were higher than previously reported. Moreover, the mortality rate was higher in patients with early suboptimal results, reflecting the bias of the decision not to review repair in higher-risk subgroups of patients. A grade of residual MR greater than 1/4 at intraoperative postrepair TEE is generally not accepted in our institution, but in these patients it was decided not to proceed with revision of the correction or with valve replacement because of the risks related to the procedure and the specific clinical conditions of the patients.

### Annular Calcification

The most frequent contraindication to ring annuloplasty in our experience was annular calcification. The idea of treating type II or III lesions by acting on leaflets, without the need for resections and annuloplasty, was appealing. Annular calcification is a worrisome challenge for the surgeon: operative mortality in patients undergoing extended decalcification procedures has been reported to be as high as 9%.<sup>12-15</sup> Unfortunately, our data show that the durability of the ringless edge-to-edge technique is suboptimal in patients with annular calcification. The probable reason why the

edge-to-edge technique failed in the calcified annulus is 2-fold. One reason is that in the presence of a calcified annulus, we accepted suboptimal results (annular calcification was correlated with higher incidence of postoperative residual MR) that eventually progressed over time and led to overt failures requiring reoperation. The other explanation for the high incidence of failures among the patients with calcified annuli is that by adopting the isolated edge-to-edge technique, we did not correct annular dilatation and deformation, which was usually present and contributing to the mechanism of regurgitation in most patients. Annular calcification is probably the effect rather than the cause of annular dilatation, and it is caused by the altered stress distribution over the base of the leaflets.<sup>10,15</sup> Moreover, by omitting annular remodeling, we left unchanged the overload on valve and annular tissues, predisposing to further annular dilatation and leaflet disease. In a computer model of the edge-to-edge technique, we found that stress distribution to the leaflets after the edge-to-edge technique was higher when annular dilatation was not concomitantly corrected.<sup>16</sup>

### Central Versus Paracommissural Repair

No failures were recorded in patients with commissural repair; however, the position of the edge-to-edge suture was not found to be a statistically significant risk factor for reoperation. This finding could be related to the small number of patients who received the commissural repair but most probably to the fact that only one patient with commissural repair had associated annular calcification.

### Edge-to-Edge Repair Done as a Bailout Procedure

The edge-to-edge technique has been proposed as a rescue procedure by Gatti and coworkers.<sup>17</sup> However, in our experience of 5 patients who underwent the edge-to-edge technique as a rescue procedure, 2 required reoperation in the follow-up period. This variable was a strong predictor of late failure at univariable and multivariable analysis.

There are some drawbacks to the use of the edge-to-edge procedure to correct a previous attempt at valve repair. First, usually it ends with a very small orifice area, especially when it is applied to correct a previous resection. Moreover, a specific scenario that includes misinterpretation of the mechanisms of MR, as well as wrong surgical decision making, biases the results of the technique in this context.

### Predictive Value of Water Testing

Most of the failures in the follow-up period could be predicted by means of intraoperative water testing. This simple maneuver, often overlooked, was, together with the rescue procedure, the strongest predictor at multivariable analysis

of both early and late failure. In most cases, because of the overall clinical scenario and the anatomic complexity of the valve lesions, a suboptimal water-testing result was considered acceptable. In several cases the edge-to-edge technique was acutely associated with a significant reduction of valve regurgitation, which was considered an acceptable outcome in complex situations, such as in the presence of a severely calcified annulus. Unfortunately, because the valve repair was unsupported by annuloplasty, there was a significant progression of the regurgitation grade in those patients with acutely suboptimal results.

Therefore, particularly when annuloplasty is not added to the repair procedure, only optimal competence of the valve should be considered acceptable to avoid the risk of late progression of the disease with recurrence of severe regurgitation and need for reoperation.

### Limitations

Data were retrospectively collected with all possible limitations related to this model of analysis. The study group was small and highly heterogeneous. In only a few cases was the decision to avoid ring annuloplasty intentional, mostly in the presence of a small annulus and always to avoid postoperative stenosis. Considering that routine valve repair in our institution includes mitral annuloplasty, there was a strong bias of selection for the ringless annuloplasty in those patients with the most unfavorable clinical or anatomic conditions. Only midterm results were available for analysis, and longer follow-up is needed to obtain enough data for definitive inferences on the effects of ringless edge-to-edge repair.

### Conclusions

In addition to the abovementioned limitations, the present study confirms previous evidence that edge-to-edge repair offers better results when associated with ring annuloplasty. The ringless edge-to-edge technique is not effective in cases of extensively calcified annulus, in which leaflet lesions can be effectively corrected by using the technique, but if the annulus is left untreated, a high risk of late failure should be expected. The midterm results of the ringless edge-to-edge technique can be predicted by means of intraoperative water testing, and suboptimal results should never be accepted, even in the case of minimal residual leak.

On the other hand, when excluding patients with a severely calcified annulus, with rheumatic lesions, or having received the ringless edge-to-edge technique as a rescue procedure after a previous unsuccessful repair, results were quite satisfactory, suggesting that when annular function is preserved and when the indication for the edge-to-edge technique is correct, a ringless procedure might provide adequate results. This conclusion opens the perspective of percutaneous approaches for beating-heart correction of mi-



tral repair<sup>5,18</sup> in selected patients by using a ringless edge-to-edge technique.

We thank William N. Anderson, statistical consultant to Edwards Lifesciences, for the statistical review.

## References

- Gillinov AM, Cosgrove DM, Blackstone EH, Diaz R, Arnold JH, Lytle BW, et al. Durability of mitral valve repair for degenerative disease. *J Thorac Cardiovasc Surg.* 1998;116:734-43.
- Carpentier A. Cardiac valve surgery—the “French correction.” *J Thorac Cardiovasc Surg.* 1983;86:323-37.
- Detter C, Aybek T, Kupilik N, Fischlein T, Moritz A. Mitral valve annuloplasty: comparison of the mural annulus shortening suture (MASS) with the Carpentier-Edwards prosthetic ring. *J Heart Valve Dis.* 2000;9:478-86.
- Barlow CW, Ali ZA, Lim E, Barlow JB, Wells FC. Modified technique for mitral repair without ring annuloplasty. *Ann Thorac Surg.* 2003;75:298-300.
- Alfieri O, Elefteriades JA, Chapolini RJ, Steckel R, Allen WJ, Reed SW, et al. Novel suture device for beating-heart mitral leaflet approximation. *Ann Thorac Surg.* 2002;74:1488-93.
- Maisano F, Torracca L, Oppizzi M, Stefano PL, D’Addario G, La Canna G, et al. The edge-to-edge technique: a simplified method to correct mitral insufficiency. *Eur J Cardiothorac Surg.* 1998;13:240-5.
- Alfieri O, Maisano F, De Bonis M, Stefano PL, Torracca L, Oppizzi M, et al. The double-orifice technique in mitral valve repair: a simple solution for complex problems. *J Thorac Cardiovasc Surg.* 2001;122:674-81.
- Maisano F, Schreuder JJ, Oppizzi M, Fiorani B, Fino C, Alfieri O. The double-orifice technique as a standardized approach to treat mitral regurgitation due to severe myxomatous disease: surgical technique. *Eur J Cardiothorac Surg.* 2000;17:201-5.
- Flameng W, Herijgers P, Bogaerts K. Recurrence of mitral regurgitation after mitral valve repair in degenerative valve disease. *Circulation.* 2003;107:1609-13.
- Kunzelman KS, Reimink MS, Cochran RP. Annular dilatation increases stress in the mitral valve and delays coaptation: a finite element computer model. *Cardiovasc Surg.* 1997;5:427-34.
- Duebener LF, Wendler O, Nikoloudakis N, Georg T, Fries R, Schafers HJ. Mitral-valve repair without annuloplasty rings: results after repair of anterior leaflet versus posterior-leaflet defects using polytetrafluoroethylene sutures for chordal replacement. *Eur J Cardiothorac Surg.* 2000;17:206-12.
- David TE, Feindel CM, Armstrong S, Sun Z. Reconstruction of the mitral annulus. A ten-year experience. *J Thorac Cardiovasc Surg.* 1995;110:1323-32.
- Fasol R, Mahdjoobian K, Joubert-Hubner E. Mitral repair in patients with severely calcified annulus: feasibility, surgery and results. *J Heart Valve Dis.* 2002;11:153-9.
- Ng CK, Punzengruber C, Pachinger O, Nesser J, Auer H, Franke H, et al. Valve repair in mitral regurgitation complicated by severe annulus calcification. *Ann Thorac Surg.* 2000;70:53-8.
- Carpentier AF, Pellerin M, Fuzellier JF, Relland JY. Extensive calcification of the mitral valve annulus: pathology and surgical management. *J Thorac Cardiovasc Surg.* 1996;111:718-29.
- Votta E, Maisano F, Soncini M, Redaelli A, Montevecchi FM, Alfieri O. 3-D computational analysis of the stress distribution on the leaflets after edge-to-edge repair of mitral regurgitation. *J Heart Valve Dis.* 2002;11:810-22.
- Gatti G, Cardu G, Trane R, Pugliese P. The edge-to-edge technique as a trick to rescue an imperfect mitral valve repair. *Eur J Cardiothorac Surg.* 2002;22:817-20.
- Block PC. Percutaneous mitral valve repair for mitral regurgitation. *J Interv Cardiol.* 2003;16:93-6.

## Discussion

**Dr W. Randolph Chitwood (Greenville, NC).** I congratulate Drs Maisano and Alfieri’s group for their continuing critical analysis of their patients who have undergone edge-to-edge mitral valve repair. I thank them for allowing me to review their excellent manuscript in advance.

Their earlier studies have shown good results in patients with both single and bileaflet prolapse in which the edge-to-edge method was combined with an annuloplasty ring. Generally, the group has used a complete remodeling ring to support the repair and remodel the annulus. Kunzelman and others have shown that remodeling annuloplasties provide both lower stress along the posterior annulus and better coaptation of the leaflets below the annular plane. More leaflet coaptation eventuates in lower stress on leaflet edges.

In this excellent article Dr Maisano describes 81 patients in whom the annuloplasty ring was omitted with an edge-to-edge repair for a variety of reasons. Of these patients, 60 had leaflet prolapse, 6 had normal leaflet motion but with annular dilatation and a central leak, and the remaining 15 had restrictive leaflet motion. In 32 patients severe annular calcification prevented annuloplasty ring implantation. Double-orifice repairs were done in 85%, and in the remaining 15% paracommissural approximations were done. The survival rate was 85% at 4 years, which is lower than that of other series with lone mitral disease. It is most important to note that 9 patients required reoperation.

Patients had significantly higher failure rates when the annulus was even partially calcified and not just with bar calcium. Interestingly, these patients had only trivial leaks, as determined by means of the immediate postoperative transesophageal study. Without calcification, double-orifice repairs had a 95% success rate at 4 years, and no paracommissural repairs required reoperation. The patients who had progressive leakage could usually be predicted by means of the intraoperative saline test.

In summary, it seems that calcification remains a contraindication to edge-to-edge repairs because of early failure. Our group has followed a similar rationale as Dr Alfieri; that is, if the annulus is severely calcified, then it cannot dilate more and become even more deformed. However, this study suggests that the annulus is already deformed, and it still calcifies in a manner in which abnormal stresses are still transferred to chords and leaflets.

In the past, our indications for using this method without a ring have included elderly patients with a completely calcified annulus and for paracommissural bailout operations. We have always preferred to include a band or remodeling annuloplasty ring when possible. In some elderly patients with regional calcium, we have combined the edge-to-edge method with a segmental annuloplasty, deploying segments of a Dacron annuloplasty band in any soft interposing segments between the areas of calcification.

We have not seen an increase in failures in these patients using the Alfieri technique but have seen even more failures in patients with bar calcium and no band. We have had the same experience. On the basis of Dr Maisano’s study, the latter appears to be a contraindication, especially with bar calcium, when an annuloplasty band cannot be deployed.

I have 3 questions. What do you think the mechanism of failure is for the repairs that do not have annuloplasty support? Is it ruptured chords, commissural expansion, or another problem?

Would polytetrafluoroethylene chords work here? One would think that nearly pure calcium cannot remodel spontaneously.

On the basis of these data, as you begin to develop percutaneous edge-to-edge catheter-repair methods, will you always try to add percutaneous interventions or percutaneous-based annuloplasty?

What are you now doing with these patients who are at high risk for failure? Are you doing Carpentier types of annular debridement with reconstruction followed by leaflet repair and a remodeling annuloplasty? This is really the standard in taking care of calcium, as well as a repair at the same time.

I would like to congratulate Drs Maisano and Alfieri for their pioneering work and thank the Association for the opportunity of discussing this article.

**Dr Maisano.** Thank you, Dr Chitwood. I do agree with your remarks. To answer your first question, the problem of annular calcification is that the annulus is diseased. Therefore it is probably impossible to obtain good results without manipulating it. Therefore in the case of complete calcification of the annulus, probably the best solution, at least in our experience, will be to replace the valve. I do not think that chordal replacement could be a good option in these situations for the same reason why the edge-to-edge repair failed in these patients because the mechanism of failure in these patients has been excess stress applied on leaflets on an already dilated and deformed annulus.

Regarding the second question on the percutaneous approach, I think we are in a very early stage of this new application for the edge-to-edge repair, and I do not know the answer yet. I think that the idea of avoiding the annuloplasty could be a viable solution when the annular function is preserved. In the last few years, our experience with mitral repair has improved, and we are recently looking more carefully at annular function. Therefore, although I believe that you should use a ring whenever possible for open heart procedures, my vision on the percutaneous approach without annuloplasty is that there is probably a subset of patients in whom annuloplasty can be avoided.

The third question is what to do about these patients in the near future. I believe that decalcification is to be done in younger patients, when the risk of the operation is reasonable. Probably the best solution for these patients with segmental calcification of the annulus is decalcification, whereas when the annulus is completely calcified or the patient is very old, valve replacement remains a reasonable choice.

**Dr Christophe Acar** (*Paris, France*). Dr Maisano, I enjoyed your presentation very much. Although we have used the Carpentier technique over the past years and we did not find it necessary to adopt the Alfieri technique, I wish to ask you a few questions.

First of all, you mentioned that in some patients you now decide to use a prosthetic ring based on the annulus diameter. Could you let us know what sizing criteria you would estimate as being an indication for a prosthetic ring?

It seems that the Alfieri technique can be used to treat both Carpentier type II and III insufficiencies. Your series included various causes, such as degenerative, rheumatic, and ischemic disease. How does the edge-to-edge technique apply both to prolapse and restriction?

Finally, among the various mechanisms of failure, could you tell us again what was the incidence of suture dehiscence?

**Dr Maisano.** Thank you for your comments. The first question, if I understood well, is when we consider a ring annuloplasty to be necessary. Well, again, my answer is simple. I really believe that in open heart procedures an annuloplasty device has to be implanted whenever possible. Therefore at the moment I cannot tell you a cutoff value. But I really believe that in the near future we have to focus on annular function, evaluating not only the size but also the motion of the annulus to understand whether it is malfunctioning or normal and direct our decision making.

Regarding the second question, we have had quite a bit of experience in using the Alfieri technique both for prolapse lesions and for restricted motion lesions. The technique is effective in both situations.

To answer your third question about dehiscence, we never saw one patient with edge-to-edge disruption in this series. The most common reason for reoperation was annular redilatation and, more rarely, other causes, such as new prolapse lesions in segments that were not treated at the first operation.

**Dr David H. Adams** (*New York, NY*). I just wanted to start by giving you a historical perspective. My partner, Farzan Filsoufi, handed me an article a while ago that reminded me that Henry Nichols actually presented edge-to-edge repair at the 36th Annual Meeting of The American Association for Thoracic Surgery in 1956, and it was interesting. His quote was, "Leaflets are not strong enough to hold sutures under tension." He also had a few other comments. We have seen, in our limited experience with the Alfieri technique, suture breakthrough in rheumatic patients. You did not see that? Leaflets were not tearing?

**Dr Maisano.** No.

**Dr Adams.** My second question is about combined type II and type III lesions. In your abstract you note that you had patients who had type III lesions in combination with type II lesions. Is that correct?

**Dr Maisano.** We had a few patients with a combination of both mechanisms.

**Dr Adams.** That is an unusual lesion set to have type III lesions in combination with type II lesions.

**Dr Maisano.** It is not that unusual in rheumatic patients.

**Dr Adams.** The third question has to do with this risk stenosis. I think it is Dr Acar's question about whether you think there is a risk of stenosis with an annuloplasty versus the edge-to-edge technique.

**Dr Maisano.** No, I do not think so. The annuloplasty is not a risk factor for stenosis after the edge-to-edge technique. The problem of stenosis comes at the edge of the leaflets. Therefore when the orifice area at the site of the edge of the leaflets is more than 2.5 cm<sup>2</sup>, for a medium-sized person, you will not have problems of stenosis.

**Dr Adams.** I agree. My comment would be that I do not think you can create significant stenosis with an annuloplasty ring when the leaflet motion is not restricted.

My next question is about your degenerative freedom from reoperation at 76%, as well as the numbers you gave us that 17 of 81 patients have 3 to 4+ MR. Only 9 have undergone reoperation, but it sounds like 8 more have 3 to 4+ residual MR. Therefore the whole group failure rate sounds like 25%, but specifically in the abstract in your degenerative freedom from reoperation it was 76% at 5 years. What is your comment for that?

**Dr Maisano.** A confirmation that these results are really sub-optimal, but they are affected by the results in the subgroup of patients with calcification. I do not think that the degenerative disease was the problem. The problem was that we applied this technique in patients with annular calcification (even in those patients with segmental calcification) because we thought it could be a good solution. Actually, that was wrong, and that is why we now advocate another solution, not this one.

**Dr Adams.** My last comment is about your last sentence: "Although our experience is still limited, the edge-to-edge without ring annuloplasty is a viable option to treat ischemic [mitral regurgitation] in selected patients." I just would appreciate that in the context of the article presented by the Cleveland Clinic group at the Society of Thoracic Surgeons with a predicted 3-year 3 to 4+ recurrent MR rate actually with a flexible band ring and an Alfieri procedure in terms of the juxtaposition of your observation versus theirs.

**Dr Maisano.** Well, I did not want to present this message on the basis of a limited number of patients because in this study group we had only 10 patients with ischemic disease. Therefore, on the basis of these data, I would not suggest any message on ischemic disease. Nevertheless, in our experience with an echocardiography-based approach, we were very much satisfied by the use of the edge-to-edge repair in ischemic patients, especially when associated with an annuloplasty.

But we are currently running a study adopting the edge-to-edge procedure alone to fix moderate MR in ischemic patients.

**Dr Robert A. Dion** (*Leiden, The Netherlands*). Dr Maisano, congratulations for your nice presentation. I just have a technical remark. You told us that the use of the Alfieri technique is not appropriate in the presence of a massively calcified annulus, and you then recommend replacing the mitral valve. Well, in my experience replacing the valve in this situation is as difficult as anything, precisely because of the calcifications. We were also disappointed to experience that the Alfieri technique was indeed not suitable for massive calcification because, of course, an old patient with leaflet prolapse and massive annulus calcification would have been an ideal candidate. The first 3 patients had early failures. In the last 2 patients we first augmented largely the posterior leaflet with a pericardial inlay patch. In 1 patient we then used the Alfieri technique, and in the other one we placed neo-chordae (polytetrafluoroethylene). According to me, this is probably less dangerous than replacement. What do you think about that?

**Dr Maisano.** I agree with your suggestion, and I think that it is a good idea. The problem with severe annular calcification is that the annulus is already dilated. Therefore, when you use any kind of procedure acting solely on the leaflets, like the edge-to-edge procedure or chordal repair, you leave the annulus dilated. Therefore one good solution could be that of augmenting the leaflets to reestablish a normal ratio between the annular size and the quantity of tissue available for coaptation.

Probably I would use an anterior leaflet expansion more than a posterior leaflet expansion because the anterior leaflet is more suitable for such a technique in the presence of a calcified annulus.