

# Long-Term Outcomes of Mitral Valve Repair in Degenerative Valve Disease: Comparison Between Posterior and Anterior or Bileaflet Mitral Valve Prolapse

## Resultados a largo plazo de la plástica mitral en enfermedad degenerativa: prolapso posterior versus anterior o bivalvar

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### ABSTRACT

**Background:** The aim of this study is to compare the clinical and echocardiographic outcome of mitral valve repair secondary to degenerative mitral valve regurgitation in patients with posterior versus anterior or bileaflet mitral valve prolapse.

**Methods:** Between April 1997 and July 2013, 255 patients underwent surgery for moderate to severe degenerative mitral valve regurgitation: 175 had posterior mitral valve prolapse (Group 1) and 80 had anterior or bileaflet mitral valve prolapse (Group 2). There were no differences in age or sex between the groups. Clinical follow-up was completed in 95% of the cases with a mean follow-up period of  $5.6 \pm 3.8$  years and 77% completed echocardiographic follow-up with a mean of  $4.8 \pm 3.7$  years.

**Results:** The procedure was successful in 87% of cases (33 intraoperative conversions to mitral valve replacement) (Group 1: 98% vs. Group 2: 62.5%;  $p < 0.01$ ). Overall in-hospital mortality was 2.3% (6/255), and 10-year survival was  $92.0 \pm 2.1\%$  (Group 1:  $94.4\% \pm 2.2\%$  vs. Group 2:  $86.3 \pm 5.1\%$ ;  $p = 0.036$ ). At 10-year follow-up,  $95.6 \pm 1.6\%$  of patients were free from reoperation (Group 1:  $97.1 \pm 1.4\%$  vs. Group 2:  $89.7 \pm 5.0\%$ ;  $p = 0.035$ ),  $79.0 \pm 4.4\%$  remained free from moderate to severe mitral regurgitation (Group 1:  $80.8 \pm 4.8\%$  vs. Group 2:  $71.9 \pm 9.6\%$ ;  $p = 0.14$ ) and 91.2% were asymptomatic (92% Group 1 vs. 89.3% Group 2;  $p = 0.5$ ).

**Conclusions:** Patients undergoing mitral valve repair secondary to degenerative posterior mitral valve prolapse had higher survival and lower incidence or reoperation in the long-term follow-up. There were no differences in freedom from moderate to severe mitral regurgitation between both groups at 10-year follow-up.

**Key words:** Mitral Valve Surgery - Mitral Valve Insufficiency - Follow-Up Studies.

### RESUMEN

**Introducción:** Comparar la evolución clínica y ecocardiográfica de la plástica mitral secundaria a insuficiencia mitral degenerativa en pacientes con prolapso de la valva posterior versus prolapso anterior o bivalvar.

**Material y métodos:** Entre abril de 1997 y julio de 2013 fueron intervenidos 255 pacientes por insuficiencia mitral moderada / grave degenerativa. De ellos, 175 tenían compromiso de la valva posterior exclusivamente (Grupo 1) y 80 de la valva anterior o bivalvar (Grupo 2). No hubo diferencias en edad ni predominio de sexo entre los grupos. El seguimiento clínico se completó en el 95% de los casos con un promedio de  $5,6 \pm 3,8$  años y el ecocardiográfico en el 77% con un promedio de  $4,8 \pm 3,7$  años.

**Resultados:** El éxito del procedimiento se alcanzó en el 87% de los casos (33 conversiones intraoperatorias a reemplazo valvular) (Grupo 1: 98% vs. Grupo 2: 62,5%;  $p < 0,01$ ). La mortalidad hospitalaria global fue del 2,3% (6/255). La supervivencia a los 10 años fue del  $92,0 \pm 2,1\%$  (Grupo 1:  $94,4\% \pm 2,2\%$  vs. Grupo 2:  $86,3 \pm 5,1\%$ ;  $p = 0,036$ ). La libertad de reoperación a 10 años de seguimiento fue del  $95,6 \pm 1,6\%$  (Grupo 1:  $97,1 \pm 1,4\%$  vs. Grupo 2:  $89,7 \pm 5,0\%$ ;  $p = 0,035$ ). La libertad de insuficiencia mitral moderada/grave en el ecocardiograma a los 10 años fue del  $79,0 \pm 4,4\%$  (Grupo 1:  $80,8 \pm 4,8\%$  vs. Grupo 2:  $71,9 \pm 9,6\%$ ;  $p = 0,14$ ). El 91,2% de los pacientes se encontraban libres de síntomas a los 10 años (92% Grupo 1 vs. 89,3% Grupo 2;  $p = 0,5$ ).

**Conclusiones:** Los pacientes con plástica mitral secundaria a enfermedad degenerativa de la valva posterior tuvieron mayor supervivencia y una incidencia menor de reoperación en el seguimiento alejado. No hubo diferencias en libertad de insuficiencia mitral moderada/grave entre ambos grupos a 10 años de seguimiento.

**Palabras clave:** Válvula mitral/cirugía - Insuficiencia de la válvula mitral - Estudios de seguimiento.

### Abbreviations

CA	Coronary angiography	IDC	Idiopathic
IDC	Idiopathic dilated oton emission computed to angiography		

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## INTRODUCTION

Degenerative mitral valve disease is the most common cause of mitral regurgitation (MR), the most common valvular heart disease. (1, 2)

Myxomatous degeneration is a common condition, affecting 2% of the population. The pathological spectrum of myxomatous degeneration is broad, and it ranges from mild changes in the central portion of the posterior leaflet (fibroelastic deficiency) to Barlow's disease. (3, 4)

The most common finding in patients with degenerative mitral valve disease is posterior mitral valve prolapse due to chordal elongation or rupture, producing diverse degrees of MR due to insufficient coaptation of the mitral valve leaflets during ventricular contraction.

Previous studies have suggested that mitral valve repair should be the surgical procedure of choice for MR, as it optimizes postoperative ventricular function compared to mitral valve replacement, and provides better survival. (5-8)

Repair of the mitral valve posterior leaflet is a relatively simple procedure with excellent long-term outcomes. Anterior or bileaflet mitral valve prolapse are more difficult to repair, and long-term outcomes are not as successful or durable as mitral valve repair of the posterior leaflet prolapse. (9-11)

The aim of this study is to compare the clinical and echocardiographic long-term outcome of mitral valve repair in degenerative MR patients with posterior versus anterior or bileaflet mitral valve prolapse

## METHODS

We conducted a retrospective study of patients undergoing mitral valve repair between April 1997 and July 2013. During that period, out of 614 patients operated-on due to MR, 347 underwent mitral valve repair. Degenerative mitral valve disease was the etiology in 255 patients, which constituted the study population. Mitral regurgitation due to rheumatic, ischemic, infectious and functional (mitral annular dilation) etiologies were excluded from the study. Patients with associated surgery of the aortic valve, ascending aorta, coronary artery bypass grafting and MAZE procedures were included.

This population was divided into two groups for analysis: those with exclusively posterior leaflet involvement (Group 1) and patients with anterior or bileaflet mitral valve prolapse (Group 2).

The study was approved by the Institutional Ethics Committee, and each patient signed an informed consent form regarding the surgical procedure and postoperative follow-up.

### Surgical technique

Conventional median sternotomy was the most used approach, and lateral minithoracotomy was performed in 9% of cases. Cardiopulmonary bypass, aortic cross-clamping and cold blood cardioplegia were used in all cases. Mitral valve repair was performed according to the traditional technique described by Carpentier for the posterior leaflet (quadrangular resection, sliding and annulus plication) and for some initial cases of anterior leaflet prolapse (chordal transposition).

(12, 13) Most recently, we have used artificial chords made of polytetrafluoroethylene sutures (Gore-Tex®, W. L. Gore & Associates, Inc.). Mitral annuloplasty was added with different ring models in most patients.

All the procedures were performed using intraoperative Doppler echocardiography. Transesophageal echocardiography (TEE) is being used during surgery since 2000. Nowadays, intraoperative TEEs are performed by the anesthesiologists trained in this technique.

The procedure was considered successful when the mitral valve repair was effective, without MR or with mild residual MR in the operation room.

### Follow-up

Follow-up was made by telephone call by a staff trained in this type of work, who interrogated about symptoms or reoperations related with mitral valve disease. Data of visits to outpatient clinics were also collected.

Echocardiographic follow-up was performed at our institution, whenever possible. If the echocardiograms were performed at other institutions, the patients sent the results by fax or mail. Residual mitral regurgitation after mitral valve repair was evaluated by transthoracic echocardiography. Ventricular dimensions, systolic function using Simpson's rule and left atrial volume were measured. Continuous Doppler echocardiography was used to describe MR based on the direction of the regurgitant jet, flow intensity and systolic time intervals. The effective regurgitant orifice area (EROA) was calculated, whenever possible.

Jet intensity, but not the quantitative data, was considered in case of minimal or mild MR due to leaflet or implanted ring refringency. Moderate and severe MR were defined when the EROA was  $> 0.25 \text{ cm}^2$  and  $> 0.40 \text{ cm}^2$ , respectively.

Clinical follow-up was completed in 95% of cases with a mean follow-up of  $5.5 \pm 3.8$  years and 77% completed a mean echocardiographic follow-up of  $4.8 \pm 3.7$  years.

Patients converted to intraoperative mitral valve replacement were discarded from clinical and echocardiographic follow-up.

### Statistical analysis

Continuous variables are expressed as mean  $\pm$  standard deviation and categorical variables as percentage. Continuous variables were analyzed using Student's t test and the chi square test or Fisher's exact test to compare categorical variables. Survival curves were built using the Kaplan-Meier method and were compared with the log-rank test. A p value  $< 0.05$  was considered statistically significant. Statistical analysis was performed using IBM® SPSS® Statistics v21.

## RESULTS

The baseline population characteristics are described in Table 1.

There were no important differences in patient characteristics between both groups, except that patients in Group 1 were somewhat older and had greater incidence of moderate or severe ventricular dysfunction ( $p = 0.08$ ) and hypertension ( $p = 0.02$ ).

Table 2 shows intraoperative results. The procedure was successful in 87% of cases: 98% in Group 1 and 62.5% in Group 2 ( $p < 0.01$ ).

Aortic cross-clamp time and cardiopulmonary bypass time were greater in Group 2 ( $p < 0.001$ ).

**Table 1.** Baseline preoperative characteristics

	Posterior leaflet (n = 175)	Anterior leaflet or bileaflet (n = 80)	p
%	68.6	31.4	-
Age, years	62.2 ± 11.4	59.5 ± 12.4	0.08
Range	26-86	26-84	-
Men, n (%)	115 (65.7)	53 (66.2)	0.9
Hypertension, n (%)	99 (56.5)	33 (41.2)	0.02
Diabetes, n (%)	8 (4.5)	2 (2.5)	0.7
CRF, n (%)	5 (2.8)	2 (2.5)	1
COPD, n (%)	9 (5.14)	3 (3.7)	0.7
Previous AF, n (%)	23 (13.1)	14 (17.5)	0.3
Barlow's disease, n (%)	13 (7.4)	32 (40)	< 0.01
Aortic valve disease, n (%)	16 (9.1)	5 (6.2)	0.6
CAD, n (%)	30 (17.1)	11 (13.7)	0.4
Moderate/severe LVD, n (%)	18 (10.3)	3 (3.7)	0.08
Asymptomatic, n (%)	66 (37.7)	30 (37.5)	0.9
Heart failure (NYHA III-IV), n (%)	26 (14.8)	9 (11.2)	0.4
Dyspnea (NYHA III-IV), n (%)	77 (44)	28 (35)	0.1
Elective surgery, n (%)	157 (89.7)	73 (91.2)	0.7

CRF: Chronic renal failure. COPD: Chronic obstructive pulmonary disease. AF: Atrial fibrillation. LVD: Left ventricular dysfunction. CAD: Coronary artery disease. NYHA: New York Heart Association.

#### Intraoperative and follow-up mortality

Six patients died during hospitalization (2.3%). Mortality related to elective procedures was 0.87% (2 patients) and none of the asymptomatic patients died.

Multivariate analysis revealed that non-elective surgery was a predictor of overall mortality (OR 44.8, 95% CI 2.3-868.8).

During follow-up, mortality was 6.6% (17 patients), and was significantly lower in Group 1 ( $p = 0.047$ ). In the multivariate analysis, anterior leaflet or bileaflet disease were predictors of mortality (OR 2.97, 95% CI 106-8.31;  $p = 0.038$ ) (Table 3).

The 10-year overall survival was  $92.0 \pm 2.1\%$ , with significant differences between groups:  $94.4 \pm 2.2\%$  in Group 1 and  $86.3 \pm 5.1\%$  in Group 2 ( $p = 0.036$ ) (Figure 1 A).

At 10 years, 91.2% of patients were free from symptoms (92% in Group 1 vs. 89.3% in Group 2;  $p = 0.5$ ).

#### Reoperations

Eight reoperations were reported during follow-up (3.14%); four in each group. Freedom from reoperation was  $95.6 \pm 1.6\%$  (Group 1:  $97.1 \pm 1.4\%$  vs. Group 2:  $89.7 \pm 5.0\%$ ;  $p = 0.035$ ) (Figure 1 B).

The multivariate analysis did not identify any predictors of reoperation during follow-up.

#### Moderate/severe mitral regurgitation during follow-up

In 29 patients (11.3%), control echocardiograms showed recurrence of moderate/severe MR, without differ-

ences between groups. Recurrent MR was not associated with the degree of degenerative mitral disease, the type of ring used or the leaflet affected.

At 10 years,  $79.0 \pm 4.4\%$  of patients remained free from moderate to severe mitral regurgitation (Group 1:  $80.8 \pm 4.8\%$  vs. Group 2:  $71.9 \pm 9.6\%$ ;  $p = 0.14$ ) (Figure 2).

Multivariate analysis showed that use of neochords in the posterior leaflet (OR 7.2, 95% CI 1.4-36.1;  $p = 0.025$ ) was a predictor of moderate/severe MR during follow-up.

#### DISCUSSION

The population characteristics are similar to those of previous studies from centers with experience in this disease. (14, 15) An average age of 60 years, greater prevalence of men, an average 15% of associated coronary artery disease and elective priority in more than 90% of cases are similar to the results published by David et al. in a recent review. (11)

Patients with the most severe degenerative mitral valve disease, as Barlow's disease, were relatively younger and had greater anterior leaflet or bileaflet involvement, a finding similar to that of Adams et al. (16) Barlow's disease is more common in younger patients, and produces more severe disease in both leaflets and even in the mitral annulus, with annular calcification; thus, mitral valve repair is more difficult. (17)

More than one third of patients undergoing surgery did not have symptoms, and the percentage of

	Posterior leaflet (n = 175)	Anterior leaflet or bileaflet (n = 80)	p
<b>Mitral valve repair</b>			
Posterior resection*, n (%)	161 (92)	24 (30)	< 0.01
Anterior resection†, n (%)	0	6 (7.5)	0.001
Chordal transposition, n (%)	0	14 (17.4)	NA
Neochords, n (%)	1 (0.6)	53 (66.3)	< 0.001
<b>Annuloplasty</b>			
Complete ring‡, n (%)	133 (76)	55 (68.8)	0.22
Incomplete ring#, n (%)	12 (6.9)	9 (11.3)	0.24
Pericardium, n (%)	22 (12.6)	5 (6.3)	0.13
Without annulus, n (%)	8 (4.6)	11 (13.8)	0.01
<b>Associated surgeries</b>			
Maze procedure, n (%)	17 (9.7)	14 (17.5)	0.07
Aortic valve replacement, n (%)	12 (6.8)	2 (2.5)	0.2
Aortic valve repair§, n (%)	4 (2.2)	3 (3.7)	0.6
CABGS, n (%)	30 (17.1)	11 (13.7)	0.4
Aortic cross-clamp time, min, mean ± SD¶	79 ± 28.4	110.7 ± 37.6	< 0.01
CPB time, min, mean ± SD	103.8 ± 31.8	136.8 ± 42.8	< 0.01
<b>Follow-up duration</b>			
Survival, mean ± SD	6.7 ± 2.8	6.0 ± 2.7	0.1
Echocardiographic	6 ± 2.9	5.3 ± 2.8	0.23

\*Posterior resection: quadrangular resection, triangular resection, sliding. †Anterior resection: triangular resection. ‡Complete rings: semirigid rings. #Incomplete rings: flexible and semirigid rings. §Aortic valve repair: of the aortic leaflet and/or the ascending aorta. CPB: Cardiopulmonary bypass. SD: Standard deviation.

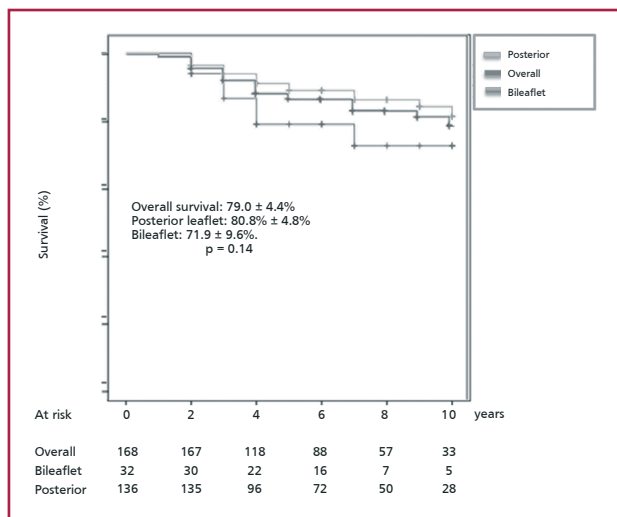
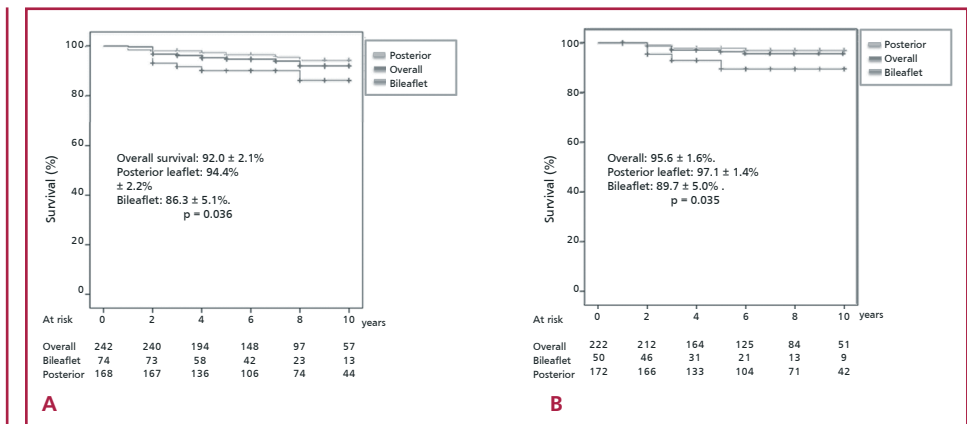
	Univariate p	p	Multivariate OR	95% CI
<b>30-day mortality</b>				
Heart failure	0.022	0.99	0.99	0.06-16.1
Non-elective surgery	0.001	0.012	44.8	2.3-868.8
Conversion	0.01	0.34	3.40	0.26-44
Anterior leaflet/bileaflet	0.02	0.055	11.2	0.95-132
Skin to skin surgical time	0.01	0.46	1.005	0.99-1.02
<b>Mortality at follow-up</b>				
Heart failure	0.007	0.17	2.65	0.65-10.7
Non-elective surgery	0.005	0.19	2.66	0.60-11.8
Anterior leaflet/bileaflet	0.047	0.038	2.97	1.06-8.31
<b>Reintervention during follow-up</b>				
Anterior mitral valve prolapse	0.02	0.21	4.28	0.43-41
Bileaflet	0.057	0.75	1.43	0.14-14
<b>Moderate/severe MR at follow-up*</b>				
Posterior neochord	0.03	0.01	7.2	1.4-36.1
Chordal transposition	0.058	0.11	0.1	0.02-1.4

\*Echocardiographic moderate/severe MR at follow-up

**Table 2.** Intraoperative and follow-up data

**Table 3.** Univariate and multivariate analyses

**Fig. 1.** Overall and leaflet-related survival. B. Global and leaflet-related freedom from reoperation



**Fig. 2.** Overall and leaflet-related freedom from moderate/severe mitral regurgitation.

asymptomatic patients was similar in both groups. In a subgroup of patients (28%) with no symptoms, absence of atrial fibrillation and normal ventricular function, severe MR was the only indication for surgery. There was no in-hospital mortality in this subgroup and mitral valve repair was successful in 87% of cases.

These data, added to the fact that non-elective surgery, generally due to class III or IV dyspnea or heart failure, were predictors of in-hospital mortality and mortality during follow-up, in this and in previous studies, support the possibility of indicating surgery in asymptomatic patients. (18)

Surgical referral of asymptomatic patients is controversial, and although surgery in patients with symptoms or in those without symptoms with ventricular dysfunction is a class I recommendation, several authors suggest that the indication should be extended to patients without symptoms and severe MR if the chance of mitral valve repair is high and the surgical center is experienced in this procedure. (16, 19, 20)

Mitral valve repair of the posterior leaflet has been possible in almost all the patients in our center. The results have also been promising in patients with anterior or bileaflet disease using Gore-Tex® neochords. Other authors propose a closer follow-up of these patients to detect minimal symptoms, especially in Barlow’ disease, before surgical referral. (21)

The number of mitral valve repairs necessary to acquire experience and improve the outcomes is also controversial. It has been suggested that surgeons should perform 25 repairs per year and centers 50 repairs per year. (22, 23) However, this is far from reality in many countries. According to the study by Grammie et al. in the United States, the range of mitral valve repairs varies from 47% to 77%, with some low-volume hospitals (22 mitral operations per year) showing high rates of mitral valve repairs, whereas other high-volume hospitals (140 operations per year) have lower rates of repairs. (24) In the United Kingdom, Anyanwu et al. reported a high mitral valve repair rate of 51%, ranging between 20% and 90%. (25). In Argentina, the reality is different and varied. The XVI CONAREC registry reported mitral valve repair in only 24% of patients with MR. (26) Conversely, a national high-volume surgical center reported mitral valve repair in 23 patients with degenerative disease per year, with favorable in-hospital and follow-up outcomes. (27) In our study, an average of 16 patients per year underwent mitral valve repair.

The use of Gore-Tex® neochords was introduced by David in 1980. (28, 29) The main problem to expand the use of this technique is the difficulty in replacing chords of appropriate length, and although several tricks have been developed to solve this problem, it is still technically demanding. (30, 31)

The long-term outcomes with the use of neochords in experienced hands have been excellent, reaching 90.2% freedom from reoperation and 91% freedom from severe mitral regurgitation by echocardiography at 18 years. (32)

Nowadays, a surgical trend advocates to “respect rather than resect” in mitral valve repair, especially

based in the routine use of neochords for anterior or posterior leaflets, with good mid- and long-term results. (16, 33, 34) We have recently began using the Gore-Tex® chords; this approach has enabled us to expand the indications of mitral valve repair for anterior and bileaflet mitral valve prolapse in a safer fashion, as in other centers worldwide. (35-37)

Overall survival was > 90% for all the groups, and mortality during follow-up was greater in patients with anterior or bileaflet mitral valve prolapse than in those with only posterior mitral valve prolapse. Anterior or bileaflet involvement was a predictor of mortality during follow-up. Both situations occur in other studies. (38, 39) The absence of long-term symptoms in > 90% of patients constitutes one of the strongest findings of this study.

Freedom from reoperation during follow-up was high and similar to that of previous publications. (38) However, moderate to severe MR by echocardiography during follow-up was greater than the reoperation rate; therefore, it is important to report this information instead of freedom from reoperation. Freedom from this complication was 80% at 10 years, a percentage similar to the risk of recurrent MR of 1-2% per year recently reported by Chikwe y Adams. (40)

Mitral regurgitation during follow-up was also greater in patients with anterior or bileaflet involvement ( $80.8 \pm 4.8\%$  vs.  $71.9 \pm 9.6\%$ ;  $p = 0.14$ ). Probably this result may be related to the difficulty in repairing this complex mitral valve disease. The results of our study were similar to those published by the most experienced authors.

The main limitations of this study are its retrospective nature and the fact that it was conducted at a single center. However, the clinical and echocardiographic data (although the latter is not complete) are attractive for our environment with little experience published in this sense, and we all know how difficult it is to follow-up patients.

## CONCLUSIONS

Mitral valve repair is a safe procedure, with low mortality and excellent long-term outcomes in terms of survival and freedom from symptoms. More than two thirds of patients with degenerative mitral valve disease have only posterior leaflet involvement; this is the most favorable situation with better outcomes for mitral valve repair. The remaining third, with anterior mitral valve prolapse of bileaflet prolapse can also benefit from mitral valve repair, because although survival and freedom from moderate/severe MR are lower during follow-up, these patients do not require long-term anticoagulation, and the need for reoperation is low. Probably, the results of mitral valve repair in more complex leaflet disease may improve with the routine use of Gore-Tex® neochords.

## Conflicts of interest

None declared.

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