

Long-term follow-up of asymptomatic or mildly symptomatic patients with severe degenerative mitral regurgitation and preserved left ventricular function

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Objectives: The timing for mitral valve surgery in asymptomatic patients with severe mitral regurgitation and preserved left ventricular function remains controversial. We analyzed the immediate and long-term outcomes of these patients after surgery.

Methods: From January 1992 to December 2012, 382 consecutive patients with severe chronic degenerative mitral regurgitation, with no or mild symptoms, and preserved left ventricular function (ejection fraction $\geq 60\%$) were submitted to surgery and followed for up to 22 years (3209 patient-years). Patients with associated surgeries, other than tricuspid valve repair, were excluded. Cox proportional-hazard survival analysis was performed to determine predictors of late mortality and mitral reoperation. Subgroup analysis involved patients with atrial fibrillation or pulmonary hypertension.

Results: Mitral valvuloplasty was performed in 98.2% of cases. Thirty-day mortality was 0.8%. Overall survival at 5, 10, and 20 years was $96.3\% \pm 1.0\%$, $89.7\% \pm 2.0\%$, and $72.4\% \pm 5.8\%$, respectively, and similar to the expected age- and gender-adjusted general population. Patients with atrial fibrillation/pulmonary hypertension had a 2-fold risk of late mortality compared with the remaining patients (hazard ratio, 2.54; 95% confidence interval, 1.17-4.80; $P = .018$). Benefit was age-dependent only in younger patients (<65 years; $P = .016$). Patients with atrial fibrillation/pulmonary hypertension (hazard ratio, 4.20, confidence interval, 1.10-11.20; $P = .037$) and patients with chordal shortening were at increased risk for reoperation, whereas patients with P2 prolapse (hazard ratio, 0.06; confidence interval, 0.008-0.51; $P = .037$) and patients with myxomatous valves (hazard ratio, 0.072; confidence interval, 0.008-0.624; $P = .017$) were at decreased risk.

Conclusions: Mitral valve repair can be achieved in the majority of patients with low mortality ($<1\%$) and excellent long-term survival. Patients with atrial fibrillation/pulmonary hypertension had compromised long-term survival, particularly younger patients (aged <65 years), and are at increased risk of mitral reoperation. (J Thorac Cardiovasc Surg 2014;148:2795-801)

Mitral valve (MV) surgery is recommended for symptomatic patients with severe primary mitral regurgitation (MR), and MV repair is the procedure of choice whenever it is feasible and expected to be durable.^{1,2} The management of patients with degenerative MR has changed dramatically during the past 2 decades, mainly because of the refinement and standardization of MV repair techniques that led to predictable and durable results. In centers of excellence, the reparability rate can reach approximately 100% and operative mortality is less than 1% in selected cases, such as isolated P2 prolapse,

and the need for reoperation because of repair failure in the long-term may be as low as 5%.³⁻⁵ Finally, the extensive knowledge of the natural history of MR and the dire consequences when it is left untreated propelled the rationale to intervene early, before complications supervene.

However, indications for mitral surgery, as expressed in the current guidelines, were based on levels of evidence B and C (consensus opinion of experts and retrospective studies), and not on randomized clinical trials (level A). This becomes even more critical in asymptomatic patients without signs of left ventricular (LV) deterioration. Two lines of thought have emerged on how to deal with this particular group of patients, one more conservative, also referred to as “watchful waiting,” mainly based on a report from Rosenhek and colleagues,⁶ who advocated delay of surgery until the end points expressed in the guidelines are reached. By contrast, others have proposed a more proactive attitude with the argument that early surgery saves the patient from the unnecessary risks associated with chronic MR.⁷ They suggest that these patients should be

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Abbreviations and Acronyms

| | |
|------|--------------------------------------|
| AF | = atrial fibrillation |
| CI | = confidence interval |
| HR | = hazard ratio |
| LV | = left ventricular |
| MR | = mitral regurgitation |
| MV | = mitral valve |
| NYHA | = New York Heart Association |
| PHT | = pulmonary hypertension |
| SPAP | = systolic pulmonary artery pressure |

referred to highly skilled centers for MV repair. Few studies have reported the long-term clinical behavior of asymptomatic patients with severe chronic MR and preserved LV function who underwent MV surgery, currently considered class IIb indications (surgery may be considered; usefulness/efficacy is less well established by evidence/opinion) in the European Guidelines¹ and class IIa (surgery should be considered; weight of evidence/opinion is in favor of usefulness/efficacy) in the American guidelines.² Therefore, we aimed at evaluating our perioperative and long-term (up to 22 years) outcomes in this population and identifying predictors of impaired survival that could lead to changes on the timing for mitral surgery.

METHODS**Patient Population and Data Collection**

From January 1992 to December 2012, 2126 patients with severe pure or predominant MR underwent MV surgery, 382 of whom were asymptomatic or mildly symptomatic, in New York Heart Association (NYHA) class I or II, and had severe degenerative MR ($\geq 3+$) and preserved LV function. These patients constitute the object of this study.

All patients underwent isolated mitral surgery, with or without concomitant tricuspid valve annuloplasty for functional regurgitation. Patients with other associated procedures were excluded from this analysis. Also excluded were patients in NYHA class III or IV, with LV ejection fraction less than 60% and LV end-systolic internal diameter 45 mm or greater, and patients with coronary artery disease, aortic valve disease, hypertrophic cardiomyopathy, ascending aortic aneurysms, and previous mitral surgery.

Data were retrieved from a dedicated database and included relevant preoperative demographic, clinical, and echocardiographic variables; surgical information; and postoperative records. A thorough investigation of all operation reports was undertaken to separate accurately the various forms of degenerative MV disease—myxomatous (including Barlow's disease), fibroelastic disease, and isolated annular dilatation—and the valve segments involved.

Myxomatous involvement was seen as those valves with thickened and opaque leaflets, moderate enlargement of the annulus, and sometimes thickened and elongated/ruptured chordae. Barlow's valves were defined as those with severe myxoid infiltration, severe annular dilatation, multiple segments of prolapse and billowing, and thin or thickened elongated chordae. Fibroelastic disease was defined as those valves with thin leaflets, fairly normal sizes, and translucence, with the exception of the prolapsed segment, and the chordae were often thin and ruptured.

Follow-up information was collected through a mailed questionnaire or by telephone interview with surviving patients, family members, or

the patient's personal physician, and included vital status and need for MV reoperation. The cumulative follow-up for the entire cohort was 3732 patient-years (mean, 8.6 ± 7.5 years; range, 0.6–21.9 years) and was complete for 98% of the patients.

Echocardiographic Evaluation

All patients had a detailed echocardiographic examination preoperatively, and Doppler examinations and the severity of MR were analyzed. In the earlier years, it was assessed qualitatively (valve morphology: flail leaflet, large coaptation defect; reversal of pulmonary vein flow) and semiquantitatively (size of the regurgitant jet in the left atrium, regurgitant jet area). In recent years, other methods, such as the vena contracta, regurgitant volume, and effective regurgitant orifice area, have been used more frequently. Left chamber dimensions, LV function (fractional shortening, ejection fraction), and systolic pulmonary artery pressure (SPAP) were measured as recommended.⁸ Intraoperative transesophageal echocardiography, both pre- and post-repair, was routinely used from the beginning of the study, and no patient left the operating room with greater than mild MR.

Operative Findings and Procedure

The operation was standardized for all patients, including cardiopulmonary bypass with moderate hypothermia (28°C – 30°C) and intermittent antegrade cold crystalloid cardioplegia through the aortic root. MV exposure was through a left atriotomy, posterior to the Waterston's groove in the majority of cases. In a few cases, the valve was reached through the right atrium and interatrial septum.

A comprehensive valve analysis of all the MV components was performed routinely. Myxomatous pathology involved 272 patients (71.2%), of whom 65 (17.0%) had severe myxomatous involvement (Barlow's disease). Isolated posterior prolapse was present in 211 patients (55.2%), isolated anterior prolapse was present in 50 patients (13.1%), and bileaflet prolapse was present in 102 patients (26.7%). Segment P2 was the most frequently involved (268 patients, 70.2%), followed by A2 (106 patients, 27.7%). Repair was oriented to correct all lesions causing mitral dysfunction, following the classic Carpentier principles.

Statistical Analysis

Continuous variables are reported as mean \pm standard deviation and compared by a Student *t* test or Mann–Whitney *U* test. Categorical variables are reported as percentages and were compared using chi-square tests. Actuarial survival and survival free of mitral reoperation were plotted using the Kaplan–Meier method, and group comparison, when available, was made using log-rank analysis. Multivariate analysis to identify independent risk factors for time-dependent events was performed using a stepwise Cox proportional hazards multivariable model and included clinical, echocardiographic, and operative variables. Criteria for entry and retention in the multivariable models were set at the 0.1 and 0.05 confidence level, respectively.

For each patient included in the study, the corresponding average age- and gender-specific annual mortality of the Portuguese general population was obtained (National Institute of Statistics, census 2012). On the basis of these mortality data, the probability of cumulative expected survival was ascertained and an expected survival curve was built. Comparison was made using a 1-sample log rank test.

A subgroup analysis was undertaken for patients with atrial fibrillation (AF) or pulmonary hypertension (PHT), defined as an SPAP at rest greater than 50 mm Hg. Patients with AF/PHT were treated as a composite covariate to be accommodated in class of IIa recommendation for mitral surgery of the American Heart Association/American College of Cardiology and European Society of Cardiology/European Association for Cardio-Thoracic Surgery guidelines. These patients were compared with the remaining patients, but because the groups were different in age

TABLE 1. Selected preoperative patient characteristics for the overall population

| Characteristics | N (%) |
|--|-------------|
| Age (mean ± SD) | 55.7 ± 14.2 |
| Male | 279 (73.0) |
| NYHA class I | 272 (71.2) |
| NYHA class II | 110 (28.8) |
| Previous stroke | 13 (3.4) |
| Hypertension | 106 (27.7) |
| Diabetes mellitus | 10 (2.6) |
| Chronic obstructive pulmonary disease | 18 (4.7) |
| AF | 64 (16.8) |
| Patients with AF or PHT | 106 (24.4) |
| Patients without AF or PHT | 276 (63.6) |
| Echocardiographic findings | |
| Tricuspid regurgitation (>2+) | 42 (9.7) |
| Ejection fraction (%) | 69.8 ± 7.5 |
| Left ventricle systolic diameter (mm) | 37.2 ± 4.2 |
| Left ventricle diastolic diameter (mm) | 62.0 ± 6.6 |
| Left atrium diameter (mm) | 50.8 ± 8.5 |
| Systolic pulmonary arterial pressure (mm Hg) | 43.0 ± 14.2 |

AF, Atrial fibrillation; NYHA, New York Heart Association; PHT, pulmonary hypertension; SD, standard deviation.

and other important demographic and clinical variables, we performed an individual matching of patients (1:1) in both groups according to age (3 years difference admitted), sex, and relevant comorbidities (renal failure, hypertension, chronic obstructive pulmonary disease, and cerebrovascular disease), obtaining 106 patients in each arm. AF and PHT (or SPAP value) were not included separately in the multivariate analysis to avoid multicollinearity with the described composite outcome. The data were analyzed using SPSS version 20 (SPSS Inc, Chicago, Ill).

RESULTS

Baseline Characteristics

The clinical and echocardiographic characteristics of the 382 patients who met the inclusion criteria are shown in Table 1. The mean age of patients was 55.5 ± 14.2 years, male gender predominated (74.7%), and 106 patients (24.4%) had AF or PHT (subgroup analysis). These patients were older (63.3 ± 11.9 years vs 52.8 ± 14 years, *P* < .0001), were more often hypertensive (35.8% vs 25.0%, *P* = .034), and had a higher incidence of fibroelastic deficiency (34.4% vs 23.2%, *P* < .0001) compared with the remaining patients. After case-matching, we obtained 2 well-balanced groups for comparison, except in their distinctive features (AF and PHT). However, patients with AF/PHT had larger left atria (56.2 vs 48.7 mm, *P* < .0001).

Details of Mitral Valve Surgery

Surgical data are presented in Table 2. MV repair was achieved in 375 patients (98.2%). Leaflet resection was performed in 271 patients (70.9%), and posterior leaflet sliding plasty was performed in 31 patients (8.1%). Artificial polytetrafluoroethylene (Gore-Tex; WL Gore & Associates Inc, Flagstaff, Ariz) chordae (initially size 4-0,

TABLE 2. Operative data of the overall population

| Characteristics | N (%) |
|-----------------------------|------------|
| MV cause/anatomy | |
| Myxomatous | 272 (71.2) |
| Barlow’s disease | 65 (17.0) |
| Fibroelastic deficiency | 96 (25.1) |
| Isolated annular dilatation | 14 (3.7) |
| Isolated anterior prolapse | 50 (13.1) |
| Isolated posterior prolapse | 211 (55.2) |
| Bileaflet prolapse | 102 (26.7) |
| Chordal rupture | 210 (55.0) |
| Surgery | |
| MV repair | 375 (98.2) |
| MV replacement | |
| Study population | 7 (1.8) |
| Study period* | 21 (3.4) |
| Ring annuloplasty | 364 (95.3) |
| Leaflet resection | 271 (70.9) |
| Artificial chordae | |
| Anterior leaflet | 109 (28.5) |
| Posterior leaflet | 30 (7.9) |
| Chordal transfer/shortening | 29 (7.4) |
| Commissural closure | 33 (8.6) |
| Papillary muscle shortening | 20 (5.2) |
| Tricuspid annuloplasty | 30 (7.9) |

MV, Mitral valve. *During the study period, 615 patients with severe MR (including all causes), without previous MV surgery, in NYHA class I/II, and with preserved LV function underwent isolated MV surgery (tricuspid repair was included).

more recently size 5-0) were implanted in 139 patients (36.4%). A prosthetic ring (Carpentier-Edwards Physio; Edwards Lifesciences Corporation, Irvine, Calif) was used in the majority of patients (95.9%), with a mean size of 32.8 mm (range, 28-38 mm). Patients with myxomatous disease had larger rings implanted (*P* < .001). A modified De Vega⁹ tricuspid annuloplasty was performed in 30 patients (7.9%).

MV replacement was necessary in 7 patients, all with intense calcium infiltration of the leaflets or mitral annulus. Four of these patients had bileaflet prolapse, but only 1 patient with Barlow’s disease had the valve replaced. The subvalvular apparatus was preserved in all but 1 patient because of heavily calcified chordae and papillary muscles.

Early Mortality and Long-Term Survival

Thirty-day mortality was 0.8% (3 patients); 1 patient died of cerebrovascular accident, and 2 patients died of cardiac causes. Overall survival at 5, 10, 15, and 20 years was 96.3% ± 1.0%, 89.7% ± 2.0%, 83.3% ± 3.0%, and 72.4% ± 5.8%, respectively. These survivals were better than those of the expected age- and gender-adjusted Portuguese standard population (Figure 1).

The Cox analysis identified age (hazard ratio [HR], 1.07; 95% confidence interval [CI], 1.03-1.11; *P* = .001), chronic pulmonary obstructive disease (HR, 3.43; 95%

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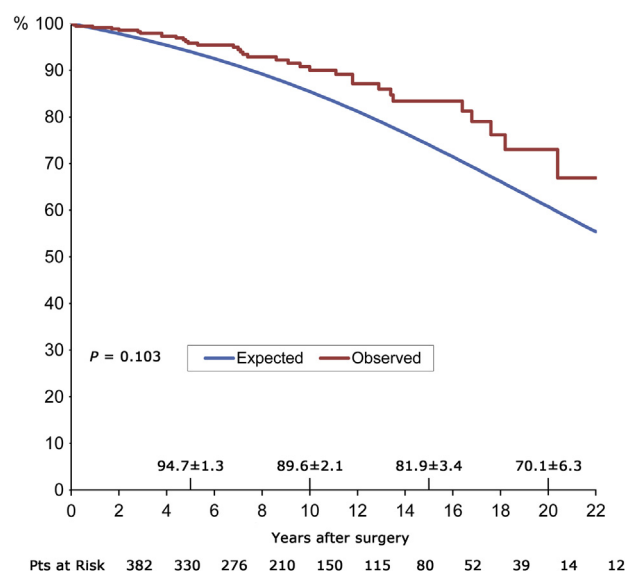


FIGURE 1. Overall survival of the study population compared with the gender- and age-matched Portuguese standard population. *Pts*, Patients.

CI, 1.30-9.05; $P = .013$), and AF/PHT (HR, 2.54; 95% CI, 1.17-4.80; $P = .018$) as independent factors of late mortality (Table 3).

Mitral Valve Reoperation

There were 2 early (in-hospital) failures of the MV repair, and in both cases we were able to re-repair and preserve the valve. Ten patients (2.6%) required MV reoperation for significant MR late after the primary procedure. The mean time from the first surgery to the reoperation was 8.6 ± 5.1 years. The valve had to be replaced in 8 cases. The main intraoperative findings were marked posterior leaflet retraction conditioning, lack of central coaptation, ring dehiscence, native and artificial chordae rupture, endocarditis with severe leaflet and chordal destruction, and leaflet calcification.

TABLE 3. Predictors of late mortality (Cox proportional hazards analysis)

| | Univariate analysis | | Multivariate analysis | |
|-------------------|---------------------|----------------|-----------------------|----------------|
| | HR (95% CI) | <i>P</i> value | HR (95% CI) | <i>P</i> value |
| Age | 1.09 (1.05-1.13) | <.0001 | 1.07 (1.03-1.11) | .001 |
| Myxomatous valves | 0.50 (0.26-6.79) | .035 | — | — |
| COPD | 4.16 (1.61-10.76) | .003 | 3.43 (1.30-9.05) | .013 |
| AF | 3.58 (1.86-6.88) | <.0001 | Not included | — |
| AF/PHT | 3.57 (1.88-6.79) | <.0001 | 2.54 (1.17-4.80) | .018 |
| TR ($\geq 2+$) | 4.08 (1.73-9.60) | .001 | — | — |
| LA dimension | 1.07 (1.03-1.11) | .001 | — | — |
| SPAP | 1.03 (1.01-1.05) | .003 | Not included | — |
| P2 prolapse | 0.47 (0.24-0.90) | .024 | — | — |

AF, Atrial fibrillation; CI, confidence interval; COPD, chronic obstructive pulmonary disease; HR, hazard ratio; LA, left atrium; PHT, pulmonary hypertension; SPAP, systolic pulmonary artery pressure; TR, tricuspid regurgitation.

TABLE 4. Predictors of mitral reoperation

| | Univariate analysis | | Multivariate analysis | |
|--------------------|---------------------|----------------|-----------------------|----------------|
| | HR (95% CI) | <i>P</i> value | HR (95% CI) | <i>P</i> value |
| Myxomatous valves | 0.16 (0.03-0.76) | .021 | 0.07 (0.01-0.62) | .017 |
| Diabetes | 2.43 (1.84-4.44) | .025 | — | — |
| AF/PHT | 3.82 (1.02-10.32) | <.0001 | 4.20 (1.10-11.20) | .037 |
| SPAP | 1.04 (1.01-1.08) | .046 | Not included | — |
| AL prolapse | 3.12 (1.80-10.67) | .001 | — | — |
| PL prolapse | 0.06 (0.01-0.26) | <.001 | — | — |
| P2 prolapse | 0.05 (0.01-0.34) | .003 | 0.06 (0.01-0.51) | .037 |
| PL resection | 0.23 (0.12-0.61) | .001 | — | — |
| Chordal shortening | 1.70 (1.23-3.12) | .014 | 9.09 (1.16-18.12) | .045 |

AF, Atrial fibrillation; AL, anterior leaflet; CI, confidence interval; HR, hazard ratio; PHT, pulmonary hypertension; PL, posterior leaflet; SPAP, systolic pulmonary artery pressure.

Freedom from mitral reoperation at 1, 10, and 20 years was $99.7\% \pm 0.3\%$, $96.5\% \pm 1.4\%$, and $93.1\% \pm 2.4\%$, respectively. Several factors were identified on the Cox analysis to independently predict the risk of reoperation (Table 4), namely, P2 prolapse (HR, 0.06; 95% CI, 0.008-0.51; $P = .037$), myxomatous valves (HR, 0.072; 95% CI, 0.008-0.624; $P = .017$), chordal tendinae shortening (HR, 9.09; 95% CI, 1.16-18.12; $P = .045$), and AF/PHT (HR, 4.20; 95% CI, 1.10-11.20; $P = .037$).

Impact of Atrial Fibrillation and Pulmonary Hypertension on Survival and Freedom From Reoperation

Patients with AF or PHT had their long-term survival compromised when compared with other asymptomatic patients without those markers (Figure 2, A). The majority of these latter patients also had normal LV systolic dimensions (210 patients with LV end-systolic diameter <40 mm). After case-matching, long-term survival at 5, 10, and 20 years was $88.8\% \pm 3.4\%$, $75.9\% \pm 5.8\%$, and $34.1\% \pm 24.4\%$, respectively, for patients with AF/PHT and $99\% \pm 1.0\%$, $97.5\% \pm 1.8\%$, and $55.7\% \pm 16.9\%$, respectively, for patients without AF/PHT ($P = .013$). The benefit of performing operation in patients without AF/PHT was not present across all ranges of ages. This advantage seemed prevalent only in younger patients (≤ 65 years) (Figure 2, B, $P = .008$). In patients aged more than 65 years, survival was similar in both groups (Figure 2, C, $P = .320$).

Patients with AF/PHT were at increased risk for mitral reoperation over time. Survival free from mitral reoperation (AF/PHT) at 20 years was $86.3\% \pm 6.9\%$ in contrast with $93.7\% \pm 3.0\%$ (Figure 3, $P = .045$).

DISCUSSION

Overall, this was a low-risk population, because patients were young, were asymptomatic or mildly symptomatic,

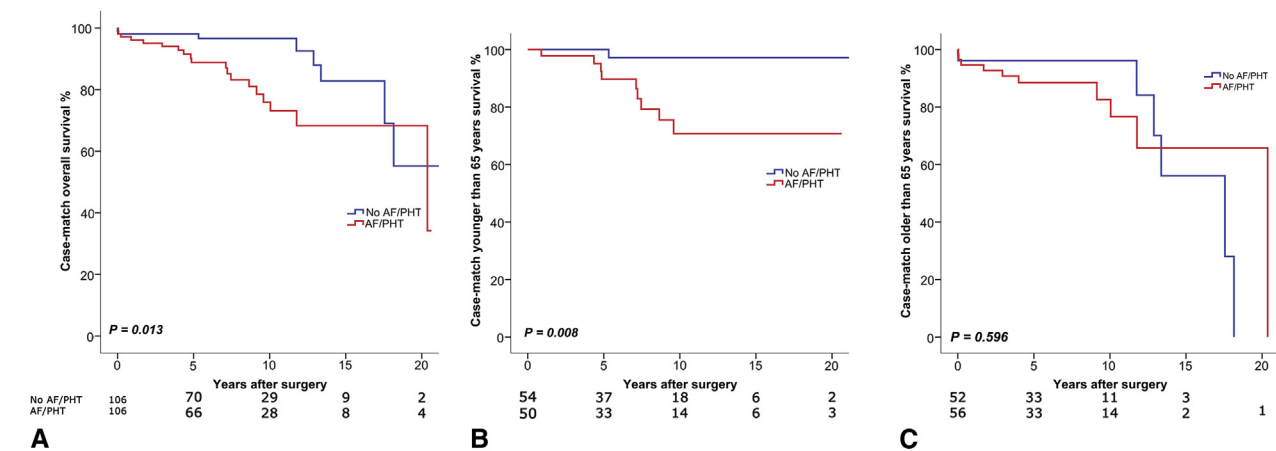


FIGURE 2. A, Overall survival in case-matched population, comparison between patients with and without AF/PHT. B, Overall survival in case-matched population aged less than 65 years. C, Overall survival in case-matched population aged more than 65 years. AF/PHT, Atrial fibrillation/pulmonary hypertension.

and had few comorbidities. Beyond that, echocardiographic parameters were suggestive of recent-onset or stable disease, because signs of LV deterioration, such as dysfunction and dilatation, were absent. Our policy on dealing with this subset of patients has been changing over time toward intervening earlier in the evolution of the disease, as experience improved, even when the guidelines gave this group a class II indication, driven by the high reparability rates achieved and low mortality.

It is now well accepted that MV repair is the procedure of choice to treat severe degenerative MR because of its undisputed advantages over valve replacement in terms of perioperative mortality, preservation of postoperative LV

function, and long-term survival.¹⁰⁻¹³ If an “early repair policy” is to be considered in asymptomatic patients with severe MR and preserved LV function, we should aim at achieving a repair rate of at least 95%, a mortality rate less than 1%, and a high durability of repair. Several studies have demonstrated the optimal long-term results of this strategy.¹⁴⁻¹⁷ Nevertheless, most of the studies have included patients with coronary artery disease, which is known to decrease survival, and few studies have evaluated on a long-term basis those patients who are outside the main surgical indications. Moreover, there is limited information regarding asymptomatic patients with preserved LV function with AF or PHT.^{18,19}

There are several logical assumptions that support this early surgery strategy, and data from our study seem to reinforce this approach. First, in patients with severe organic MR, surgery is almost unavoidable, given the time,²⁰ and the natural history of the disease has shown that if left untreated, the death rate can reach 10% to 30% per year, once symptoms ensue.²¹

Second, operating on a patient in NYHA III or IV, or with LV dysfunction or dilatation (all class I indications) implies a significant risk, with markedly higher operative and late postoperative mortality, resulting in an overall 80% increase in mortality compared with those with no or minimal symptoms.^{22,23} Our 30-day mortality was low (0.8%), probably reflecting a selected population in whom the negative consequences of chronic MR had not been established at the time of surgery.

Rosenhek and colleagues⁶ prospectively followed 132 asymptomatic patients with serial clinical and echocardiographic examinations and referred them to surgery only when the criteria described in the guidelines were fulfilled. They concluded that overall survival, including perioperative and late deaths, was not statistically different from expected survival, thus suggesting that asymptomatic

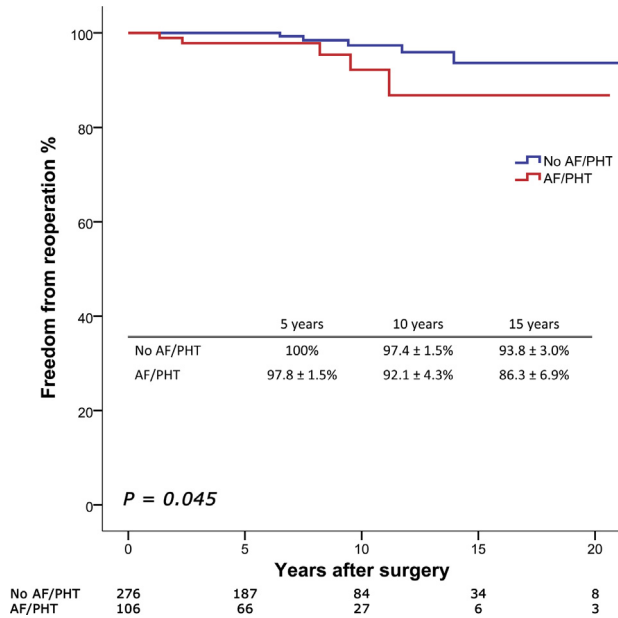


FIGURE 3. Long-term survival free from mitral reoperation, comparison between patients with and without AF/PHT. AF/PHT, Atrial fibrillation/pulmonary hypertension.

patients could be safely followed up on a regular basis (6-month intervals) until symptoms occur, or as soon as they reach the indications recommended by the guidelines. By contrast, Montant and colleagues¹⁶ reported worse postoperative and late outcomes in these subsets of patients compared with those who underwent early repair. Even patients who were closely monitored until surgical triggers appeared had an impaired late survival compared with those who had been allocated to an early surgery strategy. We must bear in mind that initial signs of incipient decompensation may easily be overlooked and the appearance of symptoms can be insidious and remain undetected, particularly in more sedentary patients.

AF and PHT are common complications of chronic MR and are associated with postoperative, cardiovascular death, and LV dysfunction.^{19,24} Current guidelines only consider them as class IIa indications in this setting, which shows that there is no clear consensus among experts to recommend early surgery in these patients.^{1,2} In the current work, we have clearly demonstrated that patients with AF/PHT had worse outcomes than patients who have not met those criteria, even after successful MV surgery. AF and PHT were identified as independent predictors of late mortality in the overall study population, with a 2-fold increased risk. Both factors may present as markers of chronicity, and it is not known whether patients recover to normal values of pulmonary artery pressure or regain sinus rhythm after surgery.

The advantage of operating on patients without AF/PHT was age-dependent, with the younger subjects (aged <65 years) deriving the most benefit. In older patients, there was no significant difference between operating earlier and the development of AF/PHT. Therefore, in this instance, a conservative approach can be pursued safely without compromising long-term survival. To the best of our knowledge, this association has not been demonstrated by others. Furthermore, patients with AF/PHT were more prone to undergo a second mitral surgery during their lifetime compared with those without AF/PHT.

A recent multicenter international study¹⁹ evaluated the outcome implications of PHT in patients with flail leaflets and found that MV surgery was beneficial but did not completely abolish the adverse effects of PHT once established (increased risk of cardiac death and heart failure). Although the majority of patients in our study could be included in the same class of indication for surgery (class IIa) in the latest 2014 American Heart Association/American College of Cardiology guidelines, patients with AF/PHT clearly represent a different risk pattern.

Third, reconstructive MV surgery is feasible in the majority of patients with degenerative MR. The rate of repair in this particular group of patients has been reported to be 80% to 100%.^{5,14-16} We repaired the MV in more than 98% of the cases, including all spectrum of degenerative

MV pathology, from fibroelastic deficiency to Barlow's disease. Most reports do not distinguish mitral pathology, and we can only speculate that myxomatous disease probably predominates in studies enrolling younger patients. This is important, because these valves, particularly Barlow's valves, are known to be more demanding and require highly differentiated expertise.²⁵ We performed MV repair in 65 of these patients, and we were unable to preserve the native valve in only 1 patient.

Fourth, MV repair has to be a durable procedure if we want to recommend it early in the clinical evolution of severe MR. It is better to have a good-functioning prosthesis than a badly repaired valve, but, in this particular scenario, replacement of the MV should be viewed as a failure. Several studies have reported outstanding longevity of the repair.^{5,26} In our study, only 12 patients required reoperation to the MV and only 2 patients had early failures (we were able to re-repair both). We have experienced 10 late failures (2.6%) after a mean of 8.7 years. At 22 years of follow-up, 93.1% of patients were free from mitral reoperation. We leave a word of caution about the occurrence of artificial chordae rupture, because it was the cause of failure in 2 patients in this series. We have previously analyzed this complication and hypothesized that instrumental manipulation could weaken the polytetrafluoroethylene.²⁷ Chordal shortening, which we have used in the early days of MV repair, was found to be an independent risk factor for reoperation. Flammeng and colleagues²⁸ also came to this conclusion. The advent of the use of artificial chordae, with consistent use of complete annuloplasty rings, allied to the increased use of intraoperative transesophageal echocardiogram to evaluate the adequacy of repair has resulted in a higher feasibility of repair and reduction of need for reoperation. On the contrary, isolated P2 prolapse was independently associated with a decreased risk of reoperation, which is similar to other reports.^{4,5}

Finally, new markers of risk in severe asymptomatic MR (before class I and IIa indications for surgery) have been described and could aid in the decision to intervene earlier or to manage those patients more conservatively. Left atrial dilatation (volume index ≥ 60 mL/m²), neurohormonal activation (elevated brain natriuretic peptide), functional capacity, and exercise-induced changes in LV volumes, ejection fraction, and SPAP all have shown important correlations with the prognosis of patients.²⁹

Study Limitations

This is a retrospective design and patients were not randomized, which can always be subject to selection bias despite the completeness of our follow-up data and the prospective nature of the database from which the data were retrieved. We do not have complete echocardiographic information during follow-up (only 65%). However, in

this young population, if relevant MR developed during the study period, patients would most likely have been sent back to surgery. Patients were deemed asymptomatic or mildly symptomatic according to the NYHA functional classification (class I or II), which has obvious intrinsic limitations. Patients preferably should have been classified on the basis of the results of an exercise test.

CONCLUSIONS

Our results show that asymptomatic or mildly symptomatic patients with severe MR and preserved LV function can be managed safely with an early surgery strategy, because it is possible to repair almost all valves, irrespective of the leaflets involved, with a mortality less than 1% and an overall survival similar to, if not better than, an age- and gender-matched population. Asymptomatic patients who have AF or PHT at the time of surgery are at increased risk for mortality and mitral reoperation compared with those who went to surgery early, before those negative markers appeared. Therefore, careful consideration should be given with regard to mitral surgery before AF/PHT is established. Older patients (aged >65 years) can be managed conservatively until conventional triggers appear without compromising late survival.

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